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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 40	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 41	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 42	Feb 13	CANCERLIT is no longer being updated
NEWS 43	Feb 24	METADEX enhancements

NEWS 44 Feb 24 PCTGEN now available on STN
NEWS 45 Feb 24 TEMA now available on STN
NEWS 46 Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 47 Feb 26 PCTFULL now contains images
NEWS 48 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 49 Mar 19 APOLLIT offering free connect time in April 2003
NEWS 50 Mar 20 EVENTLINE will be removed from STN
NEWS 51 Mar 24 PATDPAFULL now available on STN
NEWS 52 Mar 24 Additional information for trade-named substances without structures available in REGISTRY
NEWS 53 Mar 24 Indexing from 1957 to 1966 added to records in CA/CAPLUS

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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NEWS PHONE Direct Dial and Telecommunication Network Access to STN
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=> s memor? (5n) (enhanc? or improv? or recove? or restor?)
L1 19094 MEMOR? (5N) (ENHANC? OR IMPROV? OR RECOVE? OR RESTOR?)

=> s l1 (5n) (medicat? or drug? or compoun? or chemical?)
3 FILES SEARCHED...
L2 1062 L1 (5N) (MEDICAT? OR DRUG? OR COMPOUN? OR CHEMICAL?)

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=> s l2 and (diff? or unpredic? or probl?) (s) (develop? or discove?)
   3 FILES SEARCHED...
L3          24 L2 AND (DIFF? OR UNPREDIC? OR PROBL?) (S) (DEVELOP? OR DISCOVE?
               )

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           11 DUP REM L3 (13 DUPLICATES REMOVED)

=> d l4 1-11 ibib abs

L4   ANSWER 1 OF 11     MEDLINE
ACCESSION NUMBER:   2002192853     MEDLINE
DOCUMENT NUMBER:    21923975   PubMed ID: 11925852
TITLE:              Drug of abuse.
AUTHOR:             Ueki Makoto
CORPORATE SOURCE:   Doping Control Laboratory, Mitsubishi Kagaku Bio-Clinical
                    Laboratories, Inc., Itabashi-ku, Tokyo 174-8555.
SOURCE:             RINSHO BYORI. JAPANESE JOURNAL OF CLINICAL PATHOLOGY, (2002
                    Feb) 50 (2) 151-5.  Ref: 4
                    Journal code: 2984781R. ISSN: 0047-1860.
PUB. COUNTRY:       Japan
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
                    (REVIEW, TUTORIAL)
LANGUAGE:           Japanese
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200204
ENTRY DATE:         Entered STN: 20020404
                    Last Updated on STN: 20020424
                    Entered Medline: 20020423
AB   Recent development of various dietary supplements after
     enforcement of "Dietary Supplement Health and Education Act of 1994
     (DSHEA)" in the USA enabled better availability of the products through
     the Internet in Japan as well. Because of differences in the
     definitions of the term "dietary supplement" and drug control laws between
     the USA and Japan, health risks due to uncontrolled use of a drug-based
     foreign dietary supplement without a medical doctor's advice, and side
     effects due to co-administration of any problematic supplements
     with prescription drugs has become a problem in Japan. Classes
     of typical dietary supplements, the method of distribution, and known
     problems during use or overuse of these products with prescription
     drugs are discussed. Several recent positive cases are known to be due to
     the use of contaminated food supplements, which were sold not only to
     athletes but also to the general public as memory
     enhancing or anti-aging drugs. These phenomena indicate
     that trends in drug use in sports and in society becoming increasingly
     similar.

L4   ANSWER 2 OF 11     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   2002326855     MEDLINE
DOCUMENT NUMBER:    22064764   PubMed ID: 12070359
TITLE:              Barriers to Alzheimer disease drug discovery and
                    development in the biotechnology industry.
AUTHOR:             Altstiel L D
CORPORATE SOURCE:   Schering-Plough Research Institute, Kenilworth, New Jersey
                    07033-1300, USA.. larry.altstiel@spcorp.com
SOURCE:             ALZHEIMER DISEASE AND ASSOCIATED DISORDERS, (2002) 16 Suppl
                    1 S29-32.  Ref: 28
                    Journal code: 8704771. ISSN: 0893-0341.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
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General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020619
Last Updated on STN: 20020808
Entered Medline: 20020807

AB The major barrier to Alzheimer disease (AD) drug **discovery** and **development** in the biotechnology industry is scale. Most biotechnology companies do not have the personnel or expertise to carry a drug from the bench to the market. Much effort in the industry has been directed toward the elucidation of molecular mechanisms of AD and the identification of new targets. Advances in biotechnology have generated new insights into disease mechanisms, increased the number of lead compounds, and accelerated biologic screening. The majority of costs associated with drug **development** are in clinical testing and **development** activities, many of which are driven by regulatory issues. For most biotechnology companies, the costs of such trials and the infrastructure necessary to support them are prohibitive. Another significant barrier is the definition of therapeutic benefit for AD drugs; Food and Drug Administration (FDA) precedent has established that a drug must show superiority to placebo on a performance-based test of cognition and a measure of global clinical function. This restrictive definition is biased toward **drugs** that **enhance** performance on **memory**-based tests. Newer AD **drugs** are targeted toward slowing disease progression; however, there is currently no accepted definition of what constitutes efficacy in disease progression. Despite these obstacles, the biotechnology industry has much to offer AD drug **discovery** and **development**. Biotechnology firms have already **developed** essential technology for AD drug **development** and will continue to do so. Biotechnology companies can move more quickly; of course, the trick is to move quickly in the right direction. Speed may offset some of the **problems** associated with lack of scale. Additionally, biotechnology companies can afford to address markets that may be too restricted for larger pharmaceutical companies. This advantage will have increasing importance, as therapies are **developed** to address subtypes of AD.

L4 ANSWER 3 OF 11 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000278470 MEDLINE
DOCUMENT NUMBER: 20278470 PubMed ID: 10818529
TITLE: Effect of a **memory-enhancing drug**, AIT-082, on the level of synaptophysin.
AUTHOR: Lahiri D K; Ge Y W; Farlow M R
CORPORATE SOURCE: Department of Psychiatry, Indiana University School of Medicine, Indianapolis 46202, USA.. dlahiri@iupui.edu
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (2000 Apr) 903 387-93.
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000602

AB Our objective is to study the effect of AIT-082 on the level of synaptophysin in cultured pheochromocytoma (PC12) cells. The drug AIT-082, a unique purine hypoxanthine derivative, is under **development** for the treatment of Alzheimer's disease (AD). We analyzed synaptophysin

protein as an index of synaptic numbers and density and indirectly neuronal transmission. PC12 cells were treated with nerve growth factor (NGF) (50 ng/ml) and/or **different** doses of AIT-082 (5-50 ng/ml) obtained from NeoTherapeutics, CA. In the western immunoblots of conditioned media and cell lysates, we detected synaptophysin as 36-40 kDa protein bands. When PC12 cells were treated with NGF and samples were analyzed at 24 or 48 hours after treatment, the secretion of synaptophysin was drastically reduced in the conditioned medium. A significant reduction in the intracellular levels of synaptophysin in NGF-treated samples was also noted. By contrast, when PC12 cells were treated with AIT-082, the secretion of synaptophysin was increased in the conditioned medium as compared to the control. There was also a significant increase in the intracellular levels of synaptophysin in AIT-082-treated cultures. NGF treatment resulted in sympathetic neuronal phenotypes in PC12 cells. As it is known that the immunoreactivity of the synaptophysin protein correlates with the density of the synaptic terminal, our results suggest that treatment by AIT-082 could enhance neurotransmitter release at the presynaptic terminal, which may play a role in the improvement of cognition seen in AD subjects.

L4 ANSWER 4 OF 11 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3

ACCESSION NUMBER: 1999:242366 BIOSIS
DOCUMENT NUMBER: PREV199900242366
TITLE: Bridged nicotine, isonicotine, and norisonicotine effects on working memory performance of rats in the radial-arm maze.
AUTHOR(S): Levin, Edward D. (1); Damaj, M. Imad; Glassco, William; May, Everett L.; Martin, Billy R.
CORPORATE SOURCE: (1) Neurobehavioral Research Laboratory, Department of Psychiatry, Duke University Medical Center, Durham, NC, 27710 Canada
SOURCE: Drug Development Research, (Feb., 1999) Vol. 46, No. 2, pp. 107-111.
ISSN: 0272-4391.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Nicotine and other nicotinic agonists have been found to improve performance in a variety of tasks, including the radial-arm maze to improve memory. There has been an active effort to **develop** novel nicotinic agonists for the treatment of cognitive dysfunction such as is seen in Alzheimer's disease. These novel ligands can also serve as tools with which to increase our knowledge concerning the involvement of nicotinic systems with cognitive function. The current studies were conducted to assess the actions of three new nicotinic agonists, i.e., bridged nicotine, isonicotine, and norisonicotine, on choice accuracy in the radial-arm maze. Rats were trained on a win-shift working memory task in the eight-arm radial maze. In Experiment 1, the rats were administered (subcutaneously) saline and three doses of bridged nicotine, isonicotine, and norisonicotine (0.5, 1.5, and 4.5 mg/kg). Bridged nicotine did not cause any significant effects on memory performance, although it did significantly increase latency and at the high dose caused severe slowing and nonperformance. Both isonicotine and norisonicotine caused a significant linear dose-related improvement in choice accuracy, indicative of improved working memory function. In Experiment 2, another set of rats received the effective doses of 4.5 mg/kg of isonicotine and norisonicotine as well as higher doses of 13.5 mg/kg of each compound. These doses were administered alone or in combination with 5 mg/kg of the nicotinic antagonist mecamylamine to determine the nicotinic nature of the effects. As in Experiment 1 the 4.5 mg/kg of isonicotine caused a significant memory improvement. The 4.5 mg/kg dose of norisonicotine

caused a more modest rise in performance, which was not significantly **different** from control in this experiment. When both experiments were considered together, the 4.5 mg/kg doses of both isonicotine and norisonicotine were the most effective in improving working memory performance. Significant **improvements** in working **memory** were seen with both **drugs** ($P < 0.025$). The higher doses of 13.5 mg/kg of both isonicotine and norisonicotine resulted in nearly control-level performance. Thus, the typical inverted U-shaped dose-effect function was evident for both isonicotine and norisonicotine. Mecamylamine brought performance improved by the 4.5 mg/kg dose back to control levels, providing evidence for the nicotinic nature of the effect. Both isonicotine and norisonicotine show promise for **development** as **memory-improving** nicotinic agonist **drugs**.

L4 ANSWER 5 OF 11 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1998366022 MEDLINE
DOCUMENT NUMBER: 98366022 PubMed ID: 9700665
TITLE: Neurotrophic activities and therapeutic experience with a brain derived peptide preparation.
AUTHOR: Windisch M; Gschanes A; Hutter-Paier B
CORPORATE SOURCE: Institute of Experimental Pharmacology, Research Initiative Ebewe, Graz, Austria.
SOURCE: JOURNAL OF NEURAL TRANSMISSION. SUPPLEMENTUM, (1998) 53 289-98. Ref: 40
Journal code: 0425126. ISSN: 0303-6995.
PUB. COUNTRY: Austria
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981112

AB In spite that the use of naturally occurring neurotrophic factors like NGF, BDNF, CNTF, GDNF and others for treatment of neurodegenerative disorders seems promising because of their pharmacological properties, until now no large scale clinical trials have been published. One of the reasons is that these molecules are unable to penetrate through the blood brain barrier, making invasive application strategies like intracerebroventricular infusion necessary. Another one is the fact that in first clinical studies, several undesirable side-effects like hyperalgesia or weight loss have been reported. Major efforts are now put into **development** of improved application procedures and in treatment protocols for avoiding the known side-effects. Already 7 years ago it has been demonstrated that Cerebrolysin, a peptidergic drug, produced from purified brain proteins by standardized enzymatic breakdown, containing biologically active peptides, is exerting nerve growth factor like activity on neurons from dorsal root ganglia. Still ongoing investigations are showing growth promoting efficacy of this drug in **different** neuronal populations from peripheral and central nervous system. The current findings are in accordance with several older publications, enabling now a more clear interpretation of these findings. In addition to the direct neurotrophic effect, the drug also shows clear neuroprotective properties after **different** types of lesion in vitro and in vivo, resembling the pharmacological activities of naturally occurring nerve growth factors. Neurotrophic and neuroprotective efficacy has been shown with a broad variety of methods in **different** models and it is remarkable that all biochemical and morphological **drug** dependent alterations are resulting in **improvements** of learning and **memory**. Because of these experimental results,

clinical trials using cerebrolysin in Alzheimer's patients have been performed, demonstrating a quick improvement in the overall state of the patients, particularly enhancing the cognitive performance. It is remarkable that these effects are long lasting after cessation of the active treatment procedure. Even 6 months after stop of drug application improvements in AD-patients are detectable. Therefore it is concluded that cerebrolysin is able to induce repair phenomena, resulting in long term stabilization. In contrast to the naturally occurring growth factors, tolerability of this drug is extremely high, without any reports about serious side-effects in these clinical studies.

L4 ANSWER 6 OF 11 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998428683 MEDLINE
DOCUMENT NUMBER: 98428683 PubMed ID: 9753589
TITLE: Memory and the brain: unexpected chemistries and a new pharmacology.
AUTHOR: Lynch G
CORPORATE SOURCE: University of California, Irvine, California 92697-3800, USA.
SOURCE: NEUROBIOLOGY OF LEARNING AND MEMORY, (1998 Jul-Sep) 70 (1-2) 82-100. Ref: 94
Journal code: 9508166. ISSN: 1074-7427.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981110

AB Efforts to characterize long-term potentiation (LTP) and to identify its substrates have led to the **discovery** of novel synaptic chemistries, computational algorithms, and, most recently, pharmacologies. Progress has also been made in using LTP to **develop** a "standard model" of how unusual, but physiologically plausible, levels of afferent activity create lasting changes in the operating characteristics of synapses in the cortical telencephalon. Hypotheses of this type typically distinguish induction, expression, and consolidation stages in the formation of LTP. Induction involves a sequence consisting of theta-type rhythmic activity, suppression of inhibitory currents, intense synaptic depolarization, NMDA receptor activation, and calcium influx into dendritic spines. Calcium-dependent lipases, kinases, and proteases have been implicated in LTP induction. Regarding the last group, it has been recently reported that theta pattern stimulation activates calpain and that translational suppression of the protease blocks potentiation. It is thus likely that proteolysis is readily driven by synaptic activity and contributes to structural reorganization. LTP does not interact with treatments that affect transmitter release, has a markedly **differential** effect on the currents mediated by colocalized AMPA vs NMDA synaptic receptors, changes the waveform of the synaptic current, modifies the effects of drugs that modulate AMPA receptors, and is sensitive to the subunit composition of those receptors. These results indicate that LTP is expressed by changes in AMPA receptor operations. LTP is accompanied by modifications in the anatomy of synapses and spines, something which accounts for its extreme duration (weeks). As with various types of memory, LTP requires about 30 min to consolidate (become resistant to disruption). Consolidation involves adhesion chemistries and, in particular, activation of integrins, a class of transmembrane receptors that control morphology in numerous cell types. Platelet activating factor and adenosine may contribute to consolidation by regulating the engagement

of latent integrins. How consolidation stabilizes LTP expression is a topic of intense investigation but probably involves modifications to one or more of the following: membrane environment of AMPA receptors; access of regulatory proteins (e.g., kinases, proteases) to the receptors; receptor clustering; and space available for receptor insertion. Attempts to enhance LTP have focused on the induction phase and resulted in a class of centrally active drugs ("ampakines") that positively modulate AMPA receptors. These **compounds** promote LTP in vivo and **improve** the encoding of variety of **memory** types in animals. Positive results have also been obtained in preliminary studies with humans.

L4 ANSWER 7 OF 11 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94224075 EMBASE
DOCUMENT NUMBER: 1994224075
TITLE: The age-associated memory impairment construct revisited: Comments and recommendations of French-speaking workgroup.
AUTHOR: Derouesne C.; Kalafat M.; Guez D.; Malbezin M.; Poitrenaud J.; Ali Cherif A.; Alain H.; Boller F.; Danion J.M.; Dartigues J.F.; Doyon J.; Forette F.; Gauthier S.; Haw J.J.; Israel L.; Jaffard R.; Laurent B.; Lieury A.; Petit H.; et al.
CORPORATE SOURCE: Department of Neurology No 3, Hopital de la Salpetriere,F-75651 Paris Cedex 13, France
SOURCE: International Journal of Geriatric Psychiatry, (1994) 9/7 (577-587).
ISSN: 0885-6230 CODEN: IJGPES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
032 Psychiatry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB This article reports the comments and recommendations of a French-speaking workgroup concerning the controversial 'age-associated memory impairment' (AAMI) construct, proposed by Crook et al. to describe the memory **difficulties** associated with ageing. This construct's relevance and validity seem doubtful, and our workgroup met to discuss (i) the proposed causal link between age-associated memory changes and biological cerebral ageing, (ii) the psychometric criteria which could improve objective evaluation of age-related memory impairment (the initial AAMI definition criteria being inadequate), (iii) the **problems** associated with, and the clinical realities and implications of, 'memory complaint' in the elderly. (iv) how to improve definition and evaluation of the psychoaffective factors contributing to a decrease in memory performance, and (v) the specificity (or lack thereof) of this construct. The following conclusions were reached: (i) no definite link between age-associated memory changes and biological cerebral ageing has been demonstrated in either humans or animals, and therefore remains a hypothesis; (ii) objective evaluation of age-related memory impairment could be improved by comparing subjects with both more appropriately defined, education-matched young subjects (age: 25-34) and education-matched subjects of the same age. No agreement was reached concerning the validity of existing global tests, or concerning which and how many of them should be used to detect AAMI, however, both verbal and non-verbal tests should be employed and more specific memory tests with adequate validity need to be **developed**. Specific tests were proposed to improve detection of decreased memory performance, (iii) subjective memory complaints in the elderly are not exclusively dependent on decreased memory performance and have multiple and complex determinants - the role of certain psychoaffective factors, such as anxiety, has been

relatively underestimated; (iv) improved detection of the many factors contributing to decreased memory performance could be achieved by better patient screening, and (v) AAMI cannot currently be considered a specific disease entity. Should the AAMI construct be used to select patients for **memory-enhancer drug** trials, our workgroup proposed classifying elderly subjects into five groups according to the presence or absence of memory complaint, and memory performance compared with education-matched young and education- and age-matched subjects: (i) normal elderly subjects, (ii) subjects with purely subjective memory complaint (no objective impairment), (iii) subjects with memory complaint and objective impairment compared with young but not with age-matched subjects (score between one standard deviation above and below the mean of age- and education-matched controls, ie age-consistent memory impairment), (iv) subjects with memory complaint and objective impairment compared with age-matched controls (score between one and two standard deviations below the mean of age- and education-matched controls, ie late life forgetfulness), and (v) subjects with memory test performance below two standard deviations below the mean of their age- and education-matched controls, in whom organic pathology is likely in the absence of major psychoaffective disturbance.

L4 ANSWER 8 OF 11 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 92144092 MEDLINE
DOCUMENT NUMBER: 92144092 PubMed ID: 1685885
TITLE: Treatment of Alzheimer disease.
AUTHOR: Whitehouse P J
CORPORATE SOURCE: Alzheimer Center, University Hospitals of Cleveland, Ohio 44106.
SOURCE: ALZHEIMER DISEASE AND ASSOCIATED DISORDERS, (1991) 5 Suppl 1 S32-6. Ref: 11
Journal code: 8704771. ISSN: 0893-0341.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920405
Last Updated on STN: 19980206
Entered Medline: 19920319

AB Alzheimer disease (AD) and related dementias are major social **problems** threatening the lives of individuals and families and the viability of health care systems around the world. Advances in biological research are beginning to pay off with both short-term and long-term strategies for the **development** of more effective medications. Short-term strategies are aimed at treating the primary cognitive symptoms in AD as well as the secondary behavioral disturbances that occur frequently. Short-term strategies include drugs that act on cholinergic systems, including muscarinic agonists and cholinesterase inhibitors, to **improve memory** and perhaps attention. **Drugs** that act through bioaminergic systems may be useful in treating the behavioral symptoms. Long-term strategies for drug **development** are focusing on medications that may slow the progression of the disease. Growth factors and drugs that may act through other mechanisms to prevent alterations in cell metabolism offer the hope of actually preventing neural degeneration.

L4 ANSWER 9 OF 11 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1990:498553 BIOSIS
DOCUMENT NUMBER: BA90:126899
TITLE: INTRACEREBROVENTRICULAR BETHANECHOL FOR ALZHEIMER'S DISEASE

VARIABLE DOSE-RELATED RESPONSES.
AUTHOR(S): READ S L; FRAZEE J; SHAPIRA J; SMITH C; CUMMINGS J L; TOMIYASU U
CORPORATE SOURCE: JOHN DOUGLAS FRENCH CENTER, 3951 KATELLA AVE., LOS ALAMITOS, CALIF. 90720.
SOURCE: ARCH NEUROL, (1990) 47 (9), 1025-1030.
CODEN: ARNEAS. ISSN: 0003-9942.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Five male patients participated in a pilot open-label study of dose-related aspects of response to intracerebroventricular bethanechol in Alzheimer's disease. No patient had remission of symptoms, but three patients improved symptomatically and on tests of memory. Improvement was evident over a restricted range of doses for each subject, and symptoms were worse at doses below and above the optimal range. There was little overlap in the range of doses producing improvement among these three. Two patients had no consistent improvement in memory, and agitation, depression, paranoia, and seizures **developed** during treatment. Qualitative **differences** and variability in dosages producing responses complicate the identification of true drug response in the treatment of Alzheimer's disease.

L4 ANSWER 10 OF 11 MEDLINE
ACCESSION NUMBER: 91189596 MEDLINE
DOCUMENT NUMBER: 91189596 PubMed ID: 1964542
TITLE: [Development of **memory-improving drugs**].
Le developpement de medicaments pro-mnesiants.
AUTHOR: Allain H; Lieury A; Reymann J M; Martinet J P; Trebon P; Decombe R; Bentue-Ferrer D; Gandon J M
CORPORATE SOURCE: Laboratoire de Pharmacologie Experimentale et Clinique, CHRU, Rennes.
SOURCE: ANNALES DE MEDECINE INTERNE, (1990) 141 Suppl 1 19-25.
Ref: 67
Journal code: 0171744. ISSN: 0003-410X.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910526
Last Updated on STN: 19910526
Entered Medline: 19910507
AB Knowledge on the diverse processes involved in memory has been gained from multiple approaches, all necessary for the **development** of molecules aimed at enhancing memory. However, the neurobiological aspects of apprenticeship and memory remain to be fully elucidated. Long-term storage of information in the nervous system is under the control of glycoprotein synthesis. The chemistry of storage has been extensively studied in mollusks because of their simple neuroarchitecture. In mammals, the phenomenon of hippocampic long-term potentialization (HLTP), to a large extent linked to modification of glutamatergic transmissions, has been demonstrated. Stimulation of N-methyl-DL-aspartase (NMDA) receptors induces an influx of calcium, which is needed for HLTP maintenance, as are the activation of protein kinase C (PKC) and the synthesis of new proteins, for example calmodulin. At the molecular level, a cascade of biochemical events leads to modifications of neuronal connections, thus constituting the basis of memory. Memory-improving substances can be classified according to their theoretical mechanism of action: molecular pharmacology (agents inducing phenomena that mimic HLTP),

neurotransmission (molecules acting on the cholinergic, noradrenergic, serotoninergic, GABAergic or dopaminergic systems), pathophysiology (substances antagonizing or correcting anomalies responsible for the **memory** deficiency, i.e., the cognitive **enhancers**). The **development** of **memory-enhancing drugs** has encountered many obstacles, notably the **difficulty** in evaluating the effectiveness of a **medication** in **improving memory**. It is imperative that guidelines be established for the clinical and experimental **development** of such substances as well as the standardization of tests in animals and man.

L4 ANSWER 11 OF 11 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 91:71107 SCISEARCH
THE GENUINE ARTICLE: EU768
TITLE: DEVELOPMENT OF **MEMORY-IMPROVING DRUGS**
AUTHOR: ALLAIN H (Reprint); LIEURY A; REYMANN J M; MARTINET J P; TREBON P; DECOMBE R; BENTUEFERRER D; GANDON J M
CORPORATE SOURCE: CTR HOSP REG & UNIV PONTCHAILLOU, PHARMACOL EXPTL & CLIN LAB, F-35043 RENNES, FRANCE (Reprint); UNIV RENNES 2, PSYCHOL EXPTL LAB, F-35043 RENNES, FRANCE; BIOTRIAL, F-35043 RENNES, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: ANNALES DE MEDECINE INTERNE, (1990) Vol. 141, pp. 19-25.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: French
REFERENCE COUNT: 66

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Knowledge on the diverse processes involved in memory has been gained from multiple approaches, all neccessary for the **development** of molecules aimed at enhancing memory. However, the neurobiological aspects of apprenticeship and memory remain to be fully elucidated. Long-term storage of information in the nervous system is under the control of glycoprotein synthesis. The chemistry of storage has been extensively studied in mollusks because of their simple neuroarchitecture. In mammals, the phenomenon of hippocampic long-term potentialization (HLTP), to a large extent linked to modification of glutamatergic transmissions, has been demonstrated. Stimulation of N-methyl-DL-aspartase (NMDA) receptors induces an influx of calcium, which is needed for HLTP maintenance, as are the activation of protein kinase C (PKC) and the synthesis of new proteins, for example calmodulin. At the molecular level, a cascade of biochemical events leads to modifications of neuronal connections, thus constituting the basis of memory. Memory-improving substances can be classified according to their theoretical mechanism of action: molecular pharmacology (agents inducing phenomena that mimick HLTP), neurotransmission (molecules acting on the cholinergic, noradrenergic, serotoninergic, GABAergic or dopaminergic systems), pathophysiology (substances antagonizing or correcting anomalies responsible for the **memory** deficiency, i.e., the cognitive **enhancers**). The **development** of **memory-enhancing drugs** has encountered many obstacles, notably the **difficulty** in evaluating the effectiveness of a **medication** in **improving memory**. It is imperative that guidelines be established for the clinical and experimental **development** of such substances as well as the standardization of tests in animals and man.

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 FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 23:06:33 ON 06
    APR 2003
L1        413130 S MEMOR?
L2         13412 S L1 (2N) (DEFICI? OR DEFICIEN? OR INABILIT?)
L3             6 S L2 (S) KNOCK-OUT
L4             3 DUP REM L3 (3 DUPLICATES REMOVED)
L5            39 S L2 (5N) (RESTORE OR REPLAC? OR REPAIR)
L6            12 DUP REM L5 (27 DUPLICATES REMOVED)
L7           413 S L2 AND REVIEW/DT
L8            15 S L7 AND (RESTORE OR REPLAC? OR REPAIR)
L9            14 DUP REM L8 (1 DUPLICATE REMOVED)
L10           26 S L9 OR L6
L11           26 DUP REM L10 (0 DUPLICATES REMOVED)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 23:32:21 ON 06
     APR 2003
L12       466996 S MEMOR? OR RECALL?
L13          644 S L2 (5N) (IMPROV? OR RESTOR? OR REPAIR? OR REPLAC? OR RECOVE?
L14          637 S L13 NOT ESTROGEN?
L15          394 S L14 AND (COMPOUND? OR CHEMIC? OR SCREEN? OR TEST?)
L16          200 S L15 AND (COMPOUND? OR CHEM?)
L17          200 S L15 (5N) (COMPOUND? OR CHEM?)
L18          209 S L14 (5N) (COMPOUND? OR CHEM?)

=> s l13 (5n) (compound or chem?)
   3 FILES SEARCHED...
L19            5 L13 (5N) (COMPOUND OR CHEM?)

=> dup rem l19
PROCESSING COMPLETED FOR L19
L20            2 DUP REM L19 (3 DUPLICATES REMOVED)

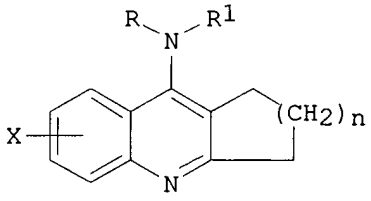
=> d l20 1-2 ibib abs

L20  ANSWER 1 OF 2  CA  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         123:83218  CA
TITLE:                    Memory enhancing 9-aminotetrahydroacridines and
                          related compounds
INVENTOR(S):              Shutske, Gregory M.; Helsley, Grover C.; Kapples,
                          Kevin J.
PATENT ASSIGNEE(S):       Hoechst-Roussel Pharmaceuticals Inc., USA
SOURCE:                   U.S., 10 pp. Cont.-in-part of U.S. Ser. No. 26,730,
                          abandoned.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     US 5391553         A    19950221       US 1988-244212    19880914
     FI 8801223         A    19880918       FI 1988-1223      19880315
     FI 91401           B    19940315
     FI 91401           C    19940627
     IL 85741           A1   19960514       IL 1988-85741     19880315
     AU 8813141         A1   19880915       AU 1988-13141     19880316
     AU 608300          B2   19910328
     DK 8801435         A    19880918       DK 1988-1435      19880316
     DK 172864          B1   19990823
     NO 8801164         A    19880919       NO 1988-1164      19880316
     NO 173498          B    19930913
```

NO 173498	C	19931222		
JP 63238063	A2	19881004	JP 1988-60665	19880316
JP 2888485	B2	19990510		
HU 46672	A2	19881128	HU 1988-1254	19880316
HU 201018	B	19900928		
ZA 8801865	A	19881130	ZA 1988-1865	19880316
CA 1318675	A1	19930601	CA 1988-561561	19880316
AU 9068239	A1	19910314	AU 1990-68239	19901219
AU 634004	B2	19930211		
AU 9068241	A1	19910314	AU 1990-68241	19901219
AU 635370	B2	19930318		
AU 9068240	A1	19910502	AU 1990-68240	19901219
AU 633668	B2	19930204		

PRIORITY APPLN. INFO.: US 1987-26730 B2 19870317
OTHER SOURCE(S): MARPAT 123:83218
GI



I

AB There are disclosed compds. having the formula I wherein n is 1-4; X is alkyl of 3-18 carbon atoms, cycloalkyl of 3-7 carbon atoms or cycloalkylloweralkyl; R is hydrogen, loweralkyl or loweralkylcarbonyl; R1 is hydrogen, loweralkyl, loweralkylcarbonyl, aryl, diloweralkylaminoloweralkyl, arylloweralkyl, diarylloweralkyl, oxygen-bridged arylloweralkyl or oxygen-bridged diarylloweralkyl; stereo isomers thereof and pharmaceutically acceptable acid addn. salts thereof, which are useful for enhancing memory, methods for synthesizing them, and pharmaceutical compns. comprising an effective memory enhancing amt. of such a compd. Thus, e.g., reaction of 9-chloro-7-cyclohexyl-1,2,3,4-tetrahydroacridine (prepn. given) with NH3 followed by salt formation afforded 9-amino-7-cyclohexyl-1,2,3,4-tetrahydroacridine hydrochloride which at 0.63 mg/kg s.c. reversed scopolamine-induced memory deficit in 20% of mice tested.

L20 ANSWER 2 OF 2 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 90358859 MEDLINE
DOCUMENT NUMBER: 90358859 PubMed ID: 2390104
TITLE: Pharmacological significance of acetylcholinesterase inhibition by tetrahydroaminoacridine.
AUTHOR: Marquis J K
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, Boston University School of Medicine, MA 02118.
SOURCE: BIOCHEMICAL PHARMACOLOGY, (1990 Sep 1) 40 (5) 1071-6. Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199009
ENTRY DATE: Entered STN: 19901026
Last Updated on STN: 19970203
Entered Medline: 19900927

AB Tetrahydroaminoacridine (THA; Tacrine) is a potent, non-competitive

inhibitor of the neuronal enzyme acetylcholinesterase (AChE) and, consequently, a potent modulator of central cholinergic function. The **compound** reportedly **improves** the **memory deficits** of Alzheimer's dementia. Experiments were run with purified bovine caudate AChE to examine the kinetic properties of THA-AChE interaction within the scheme of multiple binding sites on the enzyme and a proposed "map" of the enzyme surface. The kinetic analyses were also designed to determine whether chemical modification of peripheral anionic sites on AChE may provide insight into mechanism for selective pharmacological alteration of cholinergic function in the brain. The studies demonstrated that THA is a reversible, non-competitive inhibitor with an I50 of 160 +/- 10 nM. THA bound primarily at a hydrophobic area outside of the catalytic sites, and binding of THA enhanced the effect of Ca2+ binding to a separate group of "accelerator" sites. Experiments with Al3+ demonstrated non-competitive inhibitor effects that were additive with THA inhibition and consistent with a model suggesting interaction of THA and Al3+ at the enzyme surface. In vitro enzyme inhibition studies also provide evidence for THA "protection" of the catalytic site against inhibition by the high-affinity phosphorylating agent, DFP (isoflurophate).

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=> d his

     (FILE 'HOME' ENTERED AT 23:06:05 ON 06 APR 2003)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 23:06:33 ON 06
     APR 2003
L1       413130 S MEMOR?
L2        13412 S L1 (2N) (DEFICI? OR DEFICIEN? OR INABILIT?)
L3            6 S L2 (S) KNOCK-OUT
L4            3 DUP REM L3 (3 DUPLICATES REMOVED)
L5           39 S L2 (5N) (RESTORE OR REPLAC? OR REPAIR)
L6           12 DUP REM L5 (27 DUPLICATES REMOVED)
L7          413 S L2 AND REVIEW/DT
L8           15 S L7 AND (RESTORE OR REPLAC? OR REPAIR)
L9           14 DUP REM L8 (1 DUPLICATE REMOVED)
L10          26 S L9 OR L6
L11          26 DUP REM L10 (0 DUPLICATES REMOVED)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 23:32:21 ON 06
     APR 2003
L12      466996 S MEMOR? OR RECALL?
L13         644 S L2 (5N) (IMPROV? OR RESTOR? OR REPAIR? OR REPLAC? OR RECOVE?
L14         637 S L13 NOT ESTROGEN?
L15         394 S L14 AND (COMPOUND? OR CHEMIC? OR SCREEN? OR TEST?)
L16         200 S L15 AND (COMPOUND? OR CHEM?)
L17         200 S L15 (5N) (COMPOUND? OR CHEM?)
L18         209 S L14 (5N) (COMPOUND? OR CHEM?)
L19           5 S L13 (5N) (COMPOUND OR CHEM?)
L20           2 DUP REM L19 (3 DUPLICATES REMOVED)

=> dup rem l16
PROCESSING COMPLETED FOR L16
L21         129 DUP REM L16 (71 DUPLICATES REMOVED)

=> s l13 and (unpredict? or difficul? or problem?)
L22          31 L13 AND (UNPREDICT? OR DIFFICUL? OR PROBLEM?)

=> dup rem l22
PROCESSING COMPLETED FOR L22
L23          13 DUP REM L22 (18 DUPLICATES REMOVED)
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=> d l23 1-13 ibib abs

L23 ANSWER 1 OF 13 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2003053964 MEDLINE
DOCUMENT NUMBER: 22381820 PubMed ID: 12483218
TITLE: Selective cognitive dysfunction in acetylcholine M1 muscarinic receptor mutant mice.
AUTHOR: Anagnostaras Stephan G; Murphy Geoffrey G; Hamilton Susan E; Mitchell Scott L; Rahnama Nancy P; Nathanson Neil M; Silva Alcino J
CORPORATE SOURCE: Department of Neurobiology, Brain Research Institute, 2554 Gonda Center, Box 951761, University of California, Los Angeles, California 90095-1761, USA.
CONTRACT NUMBER: F32 AG5858 (NIA)
F32 NS10932 (NINDS)
R01 AG17499 (NIA)
R01 NS26920 (NINDS)
SOURCE: NATURE NEUROSCIENCE, (2003 Jan) 6 (1) 51-8.
Journal code: 9809671. ISSN: 1097-6256.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030205
Last Updated on STN: 20030308
Entered Medline: 20030307

AB Blockade of cholinergic neurotransmission by muscarinic receptor antagonists produces profound deficits in attention and memory. However, the antagonists used in previous studies bind to more than one of the five muscarinic receptor subtypes. Here we examined memory in mice with a null mutation of the gene coding the M1 receptor, the most densely distributed muscarinic receptor in the hippocampus and forebrain. In contrast with previous studies using nonselective pharmacological antagonists, the M1 receptor deletion produced a selective phenotype that included both **enhancements** and **deficits** in **memory**. Long-term potentiation (LTP) in response to theta burst stimulation in the hippocampus was also reduced in mutant mice. M1 null mutant mice showed normal or enhanced memory for tasks that involved matching-to-sample **problems**, but they were severely impaired in non-matching-to-sample working memory as well as consolidation. Our results suggest that the M1 receptor is specifically involved in memory processes for which the cortex and hippocampus interact.

L23 ANSWER 2 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:476838 BIOSIS
DOCUMENT NUMBER: PREV200100476838
TITLE: Effects of nicotine on memory and attention in schizophrenia.
AUTHOR(S): Myers, C. S. (1); Sherr, J. D. (1); Kakoyannis, A. (1); Robles, O. (1); Thaker, G. K. (1); Blaxton, T. A. (1)
CORPORATE SOURCE: (1) University of Maryland, Maryland Psychiatric Research Center, Baltimore, MD USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 305. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English

SUMMARY LANGUAGE: English

AB Nicotine has been shown to enhance some aspects of memory, attention and cognition in normal subjects and in some patient populations such as Alzheimer's and Parkinson's Disease groups. Memory and attentional **problems** have been consistently observed in schizophrenic (SZ) patients; this study examined whether nicotine **improves** these **deficits**. Long-term **memory** was assessed using yes/no recognition of non-nameable visuospatial designs. Working memory was assessed in a delayed match-to-sample paradigm using unfamiliar faces. The Continuous Performance Task was chosen as a measure of sustained attention. Smoking and non-smoking SZ patients and normal volunteers (NV) were tested at baseline (i.e., 2 hr nicotine abstinence) and after nicotine administration (1 mg delivered via nasal spray) in a randomized counterbalanced order. In all tasks, NVs performed better overall than SZ patients. Significant improvement following nicotine was obtained only on the long-term memory task and only for the subset of SZ patients who were smokers. In fact, nicotine administration normalized performance for SZ smokers. This memory improvement reflected a reduction in false alarm rates in the nicotine condition; hit rates were unaffected by nicotine. In contrast, no effects of nicotine were observed on working memory or attention for either subject group. These results suggest that nicotine enhances retrieval from long-term memory in SZ patients who smoke and that similar performance enhancements will not necessarily be observed for working memory and attention.

L23 ANSWER 3 OF 13 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000392175 MEDLINE
DOCUMENT NUMBER: 20342534 PubMed ID: 10880295
TITLE: Bilateral astrocytoma involving the limbic system precipitating disabling amnesia and seizures.
AUTHOR: Gillespie J S; Craig J J; McKinstry C S
CORPORATE SOURCE: Department of Neuroradiology, Royal Victoria Hospital, Grosvenor Road, Belfast, BT12 6BA, UK.
SOURCE: SEIZURE, (2000 Jun) 9 (4) 301-3.
Journal code: 9306979. ISSN: 1059-1311.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000816

AB Astrocytomas involving the limbic system are usually unilateral in nature. We report a very unusual case where a low-grade astrocytoma originating in the left temporal lobe spread to the right hippocampus through the hippocampal commissure to cause disabling amnesia and seizures. Some **improvement** in the **memory deficit** was facilitated by identification of complex partial status epilepticus. EEG should be performed in all patients with lesions of the limbic system and neuropsychological **problems** if ongoing seizure activity is not to be missed.

L23 ANSWER 4 OF 13 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000133776 MEDLINE
DOCUMENT NUMBER: 20133776 PubMed ID: 10668597
TITLE: [Heroin abuse, autobiographical memory and depression]. Heroinomanie, memoire autobiographique et depression.
AUTHOR: Eiber R; Puel M; Schmitt L
CORPORATE SOURCE: CMME, Hopital Sainte-Anne, Paris.
SOURCE: ENCEPHALE, (1999 Nov-Dec) 25 (6) 549-57.

Journal code: 7505643. ISSN: 0013-7006.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000317

AB The early psychiatric interviews with opiate addicts are characterized by three features: 1) the patient has a very factual and objective conversation, 2) the evaluation of the autobiographical memory is very **difficult**, 3) there is a high prevalence of affective disorders responsible for an impairment in cognitive functions. Therefore we have two aims: First, to compare episodic and semantic autobiographical memory in opiate addicts and healthy controls. Autobiographical memory is the knowledge a person has about oneself and his past. Personal semantic memory is the knowledge of the biographical facts, general knowledge and beliefs about oneself. Autobiographical episodic memory concerns recollections of personal events clearly delineated in time and space. Second, to estimate the impact of depression on the ability to produce autobiographical recollection in a population of opiatre addicts. Participants were consecutive attenders of a methadone outpatient clinic who are multiple drug dependent patients consuming mainly heroine. The first investigation took place in entry and after two months. We have recruited 21 patients with a mean duration of intoxication of 11 years. Ten of these patients have been investigated again after 2 months and 8 of them have been included in a methadone maintenance program. The patients'investigation comprised two parts: first, the evaluation of autobiographical memory (only assessed at entry of the study) with an autobiographical fluency test and the semi-structured autobiographical memory interview of Kopelman; second, the psychiatric assessment included self-rating questionnaires and observer-rating questionnaires. Opiate addicts showed a decrease in episodic autobiographical memory but an increase in semantic affective memory and objective modalization. In the fluency test, there was no difference in the number of evoked items between opiate addicts and healthy controls. The educational level influences several results. The possible explanations of these results are the action of the toxic products and a particular psychic functioning. The lack of correlation between autobiographical memory and affective disorder suggests the implication of the drugs in the emergence of **memory deficits**. The **improvement** of depressive symptomatology after two months occurring without psychotropic drugs suggests the transient feature of depression and emphasises on non-pharmacological aspects of treatment.

L23 ANSWER 5 OF 13 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1998414661 MEDLINE
DOCUMENT NUMBER: 98414661 PubMed ID: 9740762
TITLE: The functional neuroanatomy of episodic memory: the role of the frontal lobes, the hippocampal formation, and other areas.
AUTHOR: Desgranges B; Baron J C; Eustache F
CORPORATE SOURCE: INSERM U320 and, University of Caen, Caen Cedex, 14033, France.
SOURCE: NEUROIMAGE, (1998 Aug) 8 (2) 198-213. Ref: 120
Journal code: 9215515. ISSN: 1053-8119.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981203

AB Because it allows direct mapping of synaptic activity during behavior in the normal subject, functional neuroimaging with the activation paradigm, especially positron emission tomography, has recently provided insight into our understanding of the functional neuroanatomy of episodic memory over and above established knowledge from lesional neuropsychology. The most striking application relates to the ability to distinguish the structures implicated in the encoding and the retrieval of episodic information, as these processes are extremely **difficult** to differentiate with behavioral tasks, either in healthy subjects or in brain-damaged patients. Regarding encoding and retrieval, the results from most studies converge on the involvement of the prefrontal cortex in these processes, with a hemispheric encoding/retrieval asymmetry (HERA) such that the left side is preferentially involved in encoding, and the right in retrieval. However, there are still some questions, for instance, about bilateral activation during retrieval and a possible specialization within the prefrontal cortex. More expected from human and monkey lesional data, the hippocampal formation appears to play a role in both the encoding and the retrieval of episodic information, but the exact conditions which determine hippocampal activation and its fine-grained functional neuroanatomy have yet to be fully elucidated. Other structures are activated during episodic memory tasks, with asymmetric activation that fits the HERA model, such as preferentially left-sided activation of the association temporal and posterior cingulate areas in encoding tasks and preferentially right-sided activation of the association parietal cortex, cerebellum, and posterior cingulate in retrieval tasks. However, this hemispheric asymmetry appears to depend to some extent on the material used. These new data **enhance** our capacity to comprehend episodic **memory deficits** in neuropsychology, as well as the neural mechanisms underlying the age-related changes in episodic memory performances.

L23 ANSWER 6 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
ACCESSION NUMBER: 1998:53469 BIOSIS
DOCUMENT NUMBER: PREV199800053469
TITLE: Low folate levels in the cognitive decline of elderly patients and the efficacy of folate as a treatment for **improving memory deficits**.
AUTHOR(S): Fioravanti, M.; Ferrario, E.; Massaia, M.; Cappa, G.; Rivolta, G.; Grossi, E.; Buckley, A. E. (1)
CORPORATE SOURCE: (1) Via Antonio Bosio 28, 00161 Rome Italy
SOURCE: Archives of Gerontology and Geriatrics, (Dec., 1997) Vol. 26, No. 1, pp. 1-13.
ISSN: 0167-4943.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The relevance of low folate levels as determinants of cognitive deficits and the usefulness of folate supplementation in the treatment of cognitive deficits was reviewed from the literature. Over 40 papers and book chapters published in English, French, German, Italian and Spanish were examined. This represents those papers published in the international literature in the last 10 years which were identified by various key words including folate, cognition and aging (or ageing). Among these papers, only 13 articles specifically addressed issues relevant to the criteria adopted for this review. The remaining papers were principally concerned with depression and or with other pathologies of the aged associated with

folate deficiency. Although the specific role of low folate l
physiopathology of dementia is still under debate, a growing
emerging in the literature where low folate as well as cobala
aged patients with cognitive deficits are being considered as
functional **problems** in the absorption and utilization of
vitamins, and not merely as a sign of bad eating habits. In st
folate compounds were evaluated for treatment effects, the res
majority of investigations indicated that folate treatment was
in lessening cognitive deficits. Treatment efficacy, however,
been sufficiently demonstrated by these results because there
controlled studies and the methodology was heterogeneous for the
evaluation of cognitive characteristics. An ad hoc double-blind,
controlled versus placebo pilot study was undertaken to evaluate the
efficacy of folic acid in 30 aged patients with abnormal cognitive decline
and folate level below 3 ng/ml to better understand the value of this type
of intervention. Our results from this preliminary study demonstrated that
patients treated with folic acid for 60 days showed a significant
improvement on both memory and attention efficiency when compared with a
placebo group. The intensity of memory improvement was positively
correlated with initial severity of folate deficiency. On the contrary,
the severity of initial cognitive decline was unrelated to the degree of
folate deficiency.

L23 ANSWER 7 OF 13 MEDLINE
ACCESSION NUMBER: 95127093 MEDLINE
DOCUMENT NUMBER: 95127093 PubMed ID: 7826512
TITLE: Medial septal lesions in rats produce permanent deficits for strategy selection in a spatial memory task.
AUTHOR: Janis L S; Bishop T W; Dunbar G L
CORPORATE SOURCE: Department of Psychology, Central Michigan University.
SOURCE: BEHAVIORAL NEUROSCIENCE, (1994 Oct) 108 (5) 892-8. Journal code: 8302411. ISSN: 0735-7044.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950307
Last Updated on STN: 19950307
Entered Medline: 19950223

AB Rats with medial septal (MS) lesions have been shown to consistently use a stereotypic response strategy rather than a nonstereotypic spatial learning strategy when solving a radial maze task. The present study examined the long-term effects of MS lesions on spatial memory performance to determine whether MS lesions permanently impair rats from using a nonstereotypic strategy. Male rats, initially trained on a radial maze, were given either MS or sham surgeries and were subsequently retested on the maze. Consistent with previous studies, all rats with MS lesions used a stereotypic strategy during the postoperative retest. However, when placed through a series of retraining phases that required the rat to use a nonstereotypic strategy to solve the task, none of the MS rats could solve the task. These results indicate that lesions of the medial septum produce permanent spatial **memory deficits** that cannot be **restored** through extensive behavioral training.

L23 ANSWER 8 OF 13 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 92150489 MEDLINE
DOCUMENT NUMBER: 92150489 PubMed ID: 1784612
TITLE: Gangliosides **improve** a **memory deficit** in pentylenetetrazol-kindled rats.
AUTHOR: Grecksch G; Becker A; Gadau C; Matthies H
CORPORATE SOURCE: Institute of Pharmacology and Toxicology, Medical Academy,

Magdeburg, FDR.
SOURCE: PHARMACOLOGY, BIOCHEMISTRY AND BEHAVIOR, (1991 Jul) 39 (3) 825-8.
Journal code: 0367050. ISSN: 0091-3057.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920405
Last Updated on STN: 19920405
Entered Medline: 19920319

AB Epileptic patients often show impairments in a number of cognitive functions. Kindling is considered to be a useful experimental model for human epilepsy. Recently we have demonstrated a learning impairment in a shuttle box experiment in pentylenetetrazol (PTZ)-kindled rats. This model offers the possibility to investigate the relation between repeated convulsions and their consequences on learning and on the other side to test the effectiveness of substances on both processes. Although systemic application of gangliosides has neither an effect on the development of seizures induced by repeated injections of PTZ, nor on seizures induced by PTZ in kindled animals, the treatment protects against the memory-impairing effect of convulsions. These findings suggest a new useful strategy in the therapy of epileptic patients with the aim of diminishing the psychosocial **problems** in persons with seizure disorders: a combination of the anticonvulsive basic therapy and gangliosides.

L23 ANSWER 9 OF 13 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 91:498042 SCISEARCH
THE GENUINE ARTICLE: GD543
TITLE: GANGLIOSIDES **IMPROVE** A **MEMORY** **DEFICIT** IN PENTYLENETETRAZOL-KINDLED RATS
AUTHOR: GRECKSCH G (Reprint); BECKER A; GADAU C; MATTHIES H
CORPORATE SOURCE: MED ACAD MAGDEBURG, INST PHARMACOL & TOXICOL, LEIPZIGER STR 44, O-3090 MAGDEBURG, GERMANY (Reprint)
COUNTRY OF AUTHOR: GERMANY
SOURCE: PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR, (1991) Vol. 39, No. 3, pp. 825-828.
DOCUMENT TYPE: Note; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Epileptic patients often show impairments in a number of cognitive functions. Kindling is considered to be a useful experimental model for human epilepsy. Recently we have demonstrated a learning impairment in a shuttle box experiment in pentylenetetrazol (PTZ)-kindled rats. This model offers the possibility to investigate the relation between repeated convulsions and their consequences on learning and on the other side to test the effectiveness of substances on both processes. Although systemic application of gangliosides has neither an effect on the development of seizures induced by repeated injections of PTZ, nor on seizures induced by PTZ in kindled animals, the treatment protects against the memory-impairing effect of convulsions. These findings suggest a new useful strategy in the therapy of epileptic patients with the aim of diminishing the psychosocial **problems** in persons with seizure disorders: a combination of the anticonvulsive basic therapy and gangliosides.

L23 ANSWER 10 OF 13 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 92091981 MEDLINE

DOCUMENT NUMBER: 92091981 PubMed ID: 1836493
TITLE: Depressive **deficits** in **memory**: focusing attention **improves** subsequent recall.
COMMENT: Comment in: J Exp Psychol Gen. 1991 Sep;120(
AUTHOR: Hertel P T; Rude S S
CORPORATE SOURCE: Department of Psychology, Trinity University, Texas 78212.
CONTRACT NUMBER: RO3MH44044 (NIMH)
SOURCE: JOURNAL OF EXPERIMENTAL PSYCHOLOGY: GENERAL (3) 301-9.
Journal code: 7502587. ISSN: 0096-3445.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199201
ENTRY DATE: Entered STN: 19920216
Last Updated on STN: 19920216
Entered Medline: 19920129

AB Ss diagnosed as depressed, recovered from depression, or without a history of depression performed an unintentional learning task, followed by tests of free and forced recall. In the learning task, Ss decided whether a series of nouns sensibly completed corresponding sentence frames that varied in decision **difficulty**. For half of the Ss, the focus of attention was unconstrained by the demands of this task. The others, however, were required to repeat the targeted noun at the end of the trial as a means of focusing their attention on the task. Depressed Ss in the unfocused condition subsequently recalled fewer words than did both control groups, but this deficit disappeared in the focused condition. These results suggest that depression might not fundamentally impair the resources required for good performance on such tasks. The results' relevance to resource-allocation, initiative, and inhibition accounts of depressive deficits in memory is discussed.

L23 ANSWER 11 OF 13 MEDLINE
ACCESSION NUMBER: 91189596 MEDLINE
DOCUMENT NUMBER: 91189596 PubMed ID: 1964542
TITLE: [Development of memory-improving drugs].
Le developpement de medicaments pro-mnesiants.
AUTHOR: Allain H; Lieury A; Reymann J M; Martinet J P; Trebon P; Decombe R; Bentue-Ferrer D; Gandon J M
CORPORATE SOURCE: Laboratoire de Pharmacologie Experimentale et Clinique, CHRU, Rennes.
SOURCE: ANNALES DE MEDECINE INTERNE, (1990) 141 Suppl 1 19-25.
Ref: 67
Journal code: 0171744. ISSN: 0003-410X.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910526
Last Updated on STN: 19910526
Entered Medline: 19910507

AB Knowledge on the diverse processes involved in memory has been gained from multiple approaches, all necessary for the development of molecules aimed at enhancing memory. However, the neurobiological aspects of apprenticeship and memory remain to be fully elucidated. Long-term storage of information in the nervous system is under the control of glycoprotein synthesis. The chemistry of storage has been extensively studied in

mollusks because of their simple neuroarchitecture. In mammals, the phenomenon of hippocampic long-term potentialization (HLTP), to a large extent linked to modification of glutamatergic transmissions, has been demonstrated. Stimulation of N-methyl-DL-aspartase (NMDA) receptors induces an influx of calcium, which is needed for HLTP maintenance, as are the activation of protein kinase C (PKC) and the synthesis of new proteins, for example calmodulin. At the molecular level, a cascade of biochemical events leads to modifications of neuronal connections, thus constituting the basis of memory. Memory-improving substances can be classified according to their theoretical mechanism of action: molecular pharmacology (agents inducing phenomena that mimic HLTP), neurotransmission (molecules acting on the cholinergic, noradrenergic, serotoninergic, GABAergic or dopaminergic systems), pathophysiology (substances antagonizing or correcting anomalies responsible for the **memory deficiency**, i.e., the cognitive **enhancers**). The development of memory-enhancing drugs has encountered many obstacles, notably the **difficulty** in evaluating the effectiveness of a medication in improving memory. It is imperative that guidelines be established for the clinical and experimental development of such substances as well as the standardization of tests in animals and man.

L23 ANSWER 12 OF 13 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 91:71107 SCISEARCH
THE GENUINE ARTICLE: EU768
TITLE: DEVELOPMENT OF MEMORY-IMPROVING DRUGS
AUTHOR: ALLAIN H (Reprint); LIEURY A; REYMANN J M; MARTINET J P; TREBON P; DECOMBE R; BENTUEFERRER D; GANDON J M
CORPORATE SOURCE: CTR HOSP REG & UNIV PONTCHAILLOU, PHARMACOL EXPTL & CLIN LAB, F-35043 RENNES, FRANCE (Reprint); UNIV RENNES 2, PSYCHOL EXPTL LAB, F-35043 RENNES, FRANCE; BIOTRIAL, F-35043 RENNES, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: ANNALES DE MEDECINE INTERNE, (1990) Vol. 141, pp. 19-25.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: French
REFERENCE COUNT: 66
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Knowledge on the diverse processes involved in memory has been gained from multiple approaches, all neccessary for the development of molecules aimed at enhancing memory. However, the neurobiological aspects of apprenticeship and memory remain to be fully elucidated. Long-term storage of information in the nervous system is under the control of glycoprotein synthesis. The chemistry of storage has been extensively studied in mollusks because of their simple neuroarchitecture. In mammals, the phenomenon of hippocampic long-term potentialization (HLTP), to a large extent linked to modification of glutamatergic transmissions, has been demonstrated. Stimulation of N-methyl-DL-aspartase (NMDA) receptors induces an influx of calcium, which is needed for HLTP maintenance, as are the activation of protein kinase C (PKC) and the synthesis of new proteins, for example calmodulin. At the molecular level, a cascade of biochemical events leads to modifications of neuronal connections, thus constituting the basis of memory. Memory-improving substances can be classified according to their theoretical mechanism of action: molecular pharmacology (agents inducing phenomena that mimick HLTP), neurotransmission (molecules acting on the cholinergic, noradrenergic, serotoninergic, GABAergic or dopaminergic systems), pathophysiology (substances antagonizing or correcting anomalies responsible for the **memory deficiency**, i.e., the cognitive **enhancers**). The development of memory-enhancing drugs has encountered many obstacles, notably the **difficulty** in

evaluating the effectiveness of a medication in improving memory. It is imperative that guidelines be established for the clinical and experimental development of such substances as well as the standardization of tests in animals and man.

L23 ANSWER 13 OF 13 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 85296644 MEDLINE
DOCUMENT NUMBER: 85296644 PubMed ID: 2993944
TITLE: Neuropeptides in human memory and learning processes.
AUTHOR: Zager E L; Black P M
CONTRACT NUMBER: NS 00553 (NINDS)
SOURCE: NEUROSURGERY, (1985 Aug) 17 (2) 355-69. Ref: 177
Journal code: 7802914. ISSN: 0148-396X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198510
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19851016

AB The neuropeptides vasopressin, adrenocorticotropin (ACTH), and beta-endorphin seem to have important effects on memory and learning. Animal studies attempting to demonstrate these effects are **difficult** to interpret because of the complexity of behavior that is described as "learning" and the impossibility of assessing verbal learning in animals. This article therefore reviews some of the animal literature on neuropeptides and learning, but focuses primarily upon studies in humans, both in normal volunteers and in patients with neurological disorders. Vasopressin enhances learning under some conditions. Intranasal administration has been associated with improvement on psychometric tests in patients with mild Alzheimer's disease and Korsakoff's psychosis, although these findings are not uniform. It improves performance on memory tests in normal volunteers, but does not seem to **improve** the **memory deficit** after head trauma. Cerebrospinal fluid levels are low in patients with Alzheimer's disease. ACTH and melanocyte-stimulating hormone (MSH) are two peptides the primary behavioral effect of which seems to be on attention or goal-motivated behavior rather than on memory processes themselves. Visual discrimination and the ability to continue repetitive tasks are enhanced; in mentally retarded subjects, the administration of ACTH or MSH improves performance on a variety of neuropsychological tests. It does not, however, improve cognitive function in the elderly. Endogenous opioids including beta-endorphin and met-enkephalin seem to have primarily an amnesic effect in animal studies. Their role in human learning is still uncertain, although naloxone, which antagonizes their effects, has been associated with improved cognitive performance in patients with Alzheimer's disease. These data underscore the complexity of the processes associated with human memory and the rudimentary state of our present knowledge. Whatever the mechanisms, however, vasopressin, ACTH, and endogenous opioids seem to have important effects upon memory.

=>

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NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 40	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 41	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 42	Feb 13	CANCERLIT is no longer being updated
NEWS 43	Feb 24	METADEX enhancements

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 NEWS 44  Feb 24  PCTGEN now available on STN
 NEWS 45  Feb 24  TEMA now available on STN
 NEWS 46  Feb 26  NTIS now allows simultaneous left and right truncation
 NEWS 47  Feb 26  PCTFULL now contains images
 NEWS 48  Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results
 NEWS 49  Mar 19  APOLLIT offering free connect time in April 2003
 NEWS 50  Mar 20  EVENTLINE will be removed from STN
 NEWS 51  Mar 24  PATDPAFULL now available on STN
 NEWS 52  Mar 24  Additional information for trade-named substances without
                  structures available in REGISTRY
 NEWS 53  Mar 24  Indexing from 1957 to 1966 added to records in CA/CAPLUS

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               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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=> s memor?
L1       413130 MEMOR?

=> s l1 (2n) (defici? or deficien? or inabilit?)
L2        13412 L1 (2N) (DEFICI? OR DEFICIEN? OR INABILIT?)

=> s l2 (s) knock-out
```

L3 6 L2 (S) KNOCK-OUT

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)

=> d l4 1-4

L4 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:532607 BIOSIS
DN PREV200100532607
TI Interaction of beta amyloid with gangliosides and its role in memory in APP transgenic mice.
AU Bruchey, A. K. (1); Zhao, J. (1); Garcia, E. (1); McDonald, M. P. (1)
CS (1) Department of Pharmacology, Program in Neuroscience, Vanderbilt Univ, Nashville, TN USA
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 1136. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT Conference
LA English
SL English

L4 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:490232 BIOSIS
DN PREV200100490232
TI Age-related deficits in working memory are absent in C57BL/6 mice exposed to repeated, life-long training.
AU Murphy, G. G. (1); Silva, A. J. (1)
CS (1) Neurobiology, Psychiatry and Psychology, UCLA, Brain Res Inst, Los Angeles, CA USA
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 535. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT Conference
LA English
SL English

L4 ANSWER 3 OF 3 MEDLINE DUPLICATE 1
AN 2000299398 MEDLINE
DN 20299398 PubMed ID: 10837506
TI Strain-dependent differences in LTP and hippocampus-dependent memory in inbred mice.
AU Nguyen P V; Abel T; Kandel E R; Bourtchouladze R
CS Department of Physiology and Division of Neuroscience, University of Alberta School of Medicine, Edmonton, Canada, T6G 2H7.. erk5@columbia.edu
NC AG18199 (NIA)
SO LEARNING AND MEMORY, (2000 May-Jun) 7 (3) 170-9.
Journal code: 9435678. ISSN: 1072-0502.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000811
Last Updated on STN: 20000811
Entered Medline: 20000801

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=> d his

     (FILE 'HOME' ENTERED AT 23:06:05 ON 06 APR 2003)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 23:06:33 ON 06
     APR 2003
L1        413130 S MEMOR?
L2         13412 S L1 (2N) (DEFICI? OR DEFICIEN? OR INABILIT?)
L3             6 S L2 (S) KNOCK-OUT
L4             3 DUP REM L3 (3 DUPLICATES REMOVED)

=> s l2 (5n) (restore or replac? or repair)
L5            39 L2 (5N) (RESTORE OR REPLAC? OR REPAIR)

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6            12 DUP REM L5 (27 DUPLICATES REMOVED)

=> s l2 and review/dt
L7           413 L2 AND REVIEW/DT

=> s l7 and (restore or replac? or repair)
L8            15 L7 AND (RESTORE OR REPLAC? OR REPAIR)

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9            14 DUP REM L8 (1 DUPLICATE REMOVED)

=> l9 or l6
L9 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l9 or l6
L10           26 L9 OR L6

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11           26 DUP REM L10 (0 DUPLICATES REMOVED)

=> d l11 1-26 ibib abs'
'ABS'' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files.  Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):d l11 1-26 ibib abs
'D' IS NOT A VALID FORMAT
'L56' IS NOT A VALID FORMAT
'1-26' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files.  Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> d l11 1-26 ibib abs

L11  ANSWER 1 OF 26     MEDLINE
ACCESSION NUMBER:   2002407021     MEDLINE
DOCUMENT NUMBER:    22151279   PubMed ID: 12161513
```

TITLE: Acute modulation of aged human memory by pharmacological manipulation of glucocorticoids.
AUTHOR: Lupien S J; Wilkinson C W; Briere S; Ng Ying Kin N M K; Meaney M J; Nair N P V
CORPORATE SOURCE: Laboratory of Human Psychoneuroendocrine Research, Douglas Hospital Research Center, Department of Psychiatry, McGill University, Lasalle, Verdun, Quebec H4H-1R3, Canada.. lupson@douglas.mcgill.ca
SOURCE: JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (2002 Aug) 87 (8) 3798-807.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020806
Last Updated on STN: 20020831
Entered Medline: 20020830

AB In a previous longitudinal study of basal cortisol levels and cognitive function in humans, we showed that elderly humans with 4- to 7-yr cumulative exposure to high levels of cortisol present memory impairments, compared with elderly humans with moderate cortisol levels over years. Here, we measured whether memory performance in two groups of elderly humans separated on the basis of their cortisol history over a 5-yr period could be modulated by a hormone-replacement protocol in which we inhibited cortisol secretion by the administration of metyrapone and then restored baseline cortisol levels by infusion of hydrocortisone. We showed that in elderly subjects with a 5-yr history of moderate cortisol levels (n = 8), metyrapone treatment significantly impaired **memory** performance, a **deficit** that was reversed following hydrocortisone **replacement**. In the elderly subjects with a 5-yr history of high cortisol levels and current memory deficits (n = 9), metyrapone treatment did not have any significant effect on memory performance, but hydrocortisone treatment significantly decreased delayed memory. These results suggest that memory function in elderly humans can be intensely modulated by pharmacological manipulation of glucocorticoids, although the direction of these effects depends on the cortisol history of each individual.

L11 ANSWER 2 OF 26 MEDLINE
ACCESSION NUMBER: 2002707893 MEDLINE
DOCUMENT NUMBER: 22357495 PubMed ID: 12469866
TITLE: The lesion of the rat substantia nigra pars compacta dopaminergic neurons as a model for Parkinson's disease memory disabilities.
AUTHOR: Da Cunha Claudio; Angelucci Miriam Elizabeth Mendes; Canteras Newton S; Wonnacott Susan; Takahashi Reinaldo N
CORPORATE SOURCE: Laboratorio de Fisiologia e Farmacologia do SNC, Departamento de Farmacologia, UFPR, Curitiba, PR, Brazil.. dacunha@bio.ufpr.br
SOURCE: CELLULAR AND MOLECULAR NEUROBIOLOGY, (2002 Jun) 22 (3) 227-37. Ref: 53
Journal code: 8200709. ISSN: 0272-4340.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030109
Entered Medline: 20030108

AB 1. In this article we review the studies of memory disabilities in a rat model of Parkinson's disease (PD). 2. Intranigral administration of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) to rats causes a partial lesion in the substantia nigra, compact part (SNc) and a specific loss of dopamine and its metabolites in the striatum of rats. 3. These animals present learning and **memory deficits** but no sensorimotor impairments, thus modeling the early phase of PD when cognitive impairments are observed but the motor symptoms of the disease are barely present. 4. The cognitive deficits observed in these animals affect memory tasks proposed to model habit learning (the cued version of the water maze task and the two-way active avoidance task) and working memory (a working memory version of the water maze), but spare long-term spatial memory (the spatial reference version of the Morris water maze). 5. The treatment of these animals with levodopa in a dose that **restores** the striatal level of dopamine does not reverse these memory impairments, probably because this treatment promotes a high level of dopamine in extrastriatal brain regions, such as the prefrontal cortex and the hippocampus. 6. On the other hand, the adenosine receptor antagonist, caffeine, partly reverse the memory impairment effect of SNc lesion in these rats. This effect may be due to caffeine action on nigrostriatal neurons, since it induces dopamine release and modulates the interaction between adenosine and dopamine receptor activity. 7. These results suggest that the MPTP SNc-lesioned rats are a good model to study memory disabilities related to PD and that caffeine and other selective A(2A) adenosine receptor antagonists are promising drugs to treat this symptoms in PD patients.

L11 ANSWER 3 OF 26 MEDLINE
ACCESSION NUMBER: 2002498507 MEDLINE
DOCUMENT NUMBER: 22247397 PubMed ID: 12359512
TITLE: The social deficits of the oxytocin knockout mouse.
AUTHOR: Winslow J T; Insel T R
CORPORATE SOURCE: Center for Behavioral Neuroscience, Yerkes Regional Primate Center, Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA 30322, USA.. jwinslow@rmy.emory.edu
SOURCE: NEUROPEPTIDES, (2002 Apr-Jun) 36 (2-3) 221-9. Ref: 71
Journal code: 8103156. ISSN: 0143-4179.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20021003
Last Updated on STN: 20021214
Entered Medline: 20021126

AB Numerous studies have implicated oxytocin (OT) and oxytocin receptors in the central mediation of social cognition and social behavior. Much of our understanding of OT's central effects depends on pharmacological studies with OT agonists and antagonists. Recently, our knowledge of OT's effects has been extended by the development of oxytocin knockout (OTKO) mice. Mice with a null mutation of the OT gene manifest several interesting cognitive and behavioral changes, only some of which were predicted by pharmacological studies. Contrary to studies in rats, mice do not appear to require OT for normal sexual or maternal behavior, though OT is necessary for the milk ejection reflex during lactation. OTKO pups thrive if raised by a lactating female, but OTKO pups emit fewer ultrasonic

vocalizations with maternal separation and OTKO adults are more aggressive than WT mice. Remarkably, OTKO mice fail to recognize familiar conspecifics after repeated social encounters, though olfactory and non-social memory functions appear to be intact. Central OT administration into the amygdala **restores** social recognition. The development of transgenic mice with specific **deficits** in social **memory** represents a promising approach to examine the cellular and neural systems of social cognition. These studies may provide valuable new perspectives on diseases characterized by social deficits, such as autism or reactive attachment disorder.

L11 ANSWER 4 OF 26 MEDLINE
ACCESSION NUMBER: 2002385820 MEDLINE
DOCUMENT NUMBER: 22077806 PubMed ID: 12082224
TITLE: The role of axonal sprouting in functional reorganization after CNS injury: lessons from the hippocampal formation.
AUTHOR: Ramirez J J
CORPORATE SOURCE: Davidson College, Davidson, NC 28035, USA.. juramirez@davidson.edu
CONTRACT NUMBER: MH60608 (NIMH)
SOURCE: Restor Neurol Neurosci, (2001) 19 (3-4) 237-62. Ref: 222
Journal code: 9005499. ISSN: 0922-6028.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020724
Last Updated on STN: 20020816
Entered Medline: 20020815

AB Functional reorganization is often invoked to account for recovery of function after central nervous system (CNS) injury. The mechanisms underlying this possible reorganization, however, remain uncertain. In the last 30 years, studies of the hippocampal formation of rats have indicated that the CNS is capable of undergoing significant changes in its pattern of connectivity in response to injury. Here, we explore numerous examples of lesion-induced alterations in hippocampal connectivity known as axonal sprouting. Both homotypic and heterotypic sprouting occur in the denervated hippocampus after unilateral entorhinal cortex lesions. We assess the behavioral relevance of glutamatergic homotypic sprouting emerging from the surviving contralateral entorhinal area (i.e., the crossed temporodentate projection) as well as the heterotypic sprouting from the remaining surviving afferents (e. g., the cholinergic septodentate pathway) to the hippocampus. Studies examining the role of crossed temporodentate sprouting in recovery from **memory deficits** after entorhinal cortex injury indicate that homotypic sprouting may indeed contribute to a reorganization of cortical function resulting in recovered mnemonic capacity. Heterotypic sprouting is not as clearly linked to recovery of function after bilateral entorhinal injury. We propose a tripartite model for functional reorganization based on homotypic sprouting, neurotrophic factors, and altered inhibitory functioning to account for how relatively small increases in surviving homotypic pathways might **restore** neurological function.

L11 ANSWER 5 OF 26 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:12978 CA
TITLE: M1 muscarinic agonists: their potential in treatment and as disease-modifying agents in Alzheimer's disease
AUTHOR(S): Fisher, Abraham
CORPORATE SOURCE: Israel Institute for Biological Research, Ness-Ziona,

74100, Israel
SOURCE: Drug Development Research (2000), 50(3/4), 291-297
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 67 refs. M1-type muscarinic receptors (mAChR) have an important role in cognitive processing and are relatively unchanged in Alzheimer's disease (AD). Therefore, M1 agonists represent a rational treatment strategy in AD. However, some muscarinic agonists gave disappointing results in Phase III studies in AD patients. These agonists lacked M1 selectivity in vivo and/or had several major clin. limitations, precluding a proper testing of the clin. concept. There is now justified hope that selective M1 agonists could provide limited causal therapy in AD. Thus, a relation between the formation of .beta.-amyloid peptide and amyloid plaques, tau phosphorylation, and loss of cholinergic function in AD brains has been reported. This may shift the interest in such compds. from a mere symptomatic treatment toward their use in the future as disease-modifying agents via muscarinic regulation of .beta.-amyloid metab. and tau phosphorylation. Such characteristics can be detected in the functionally selective M1 agonists of the AF series (e.g., AF102B, AF150(S), AF267B). These M1 agonists, inter alia, **restore** cognitive impairments in several animal models of AD, promote the neurotropic and nonamyloidogenic amyloid precursor protein (APPs) processing pathways, and decrease tau protein phosphorylation. Apolipoprotein E-**deficient** mice have **memory deficits**, synaptic loss of basal forebrain cholinergic projections, and hyperphosphorylation of distinct epitopes of the microtubule-assocd. protein tau. These impairments are restored by subchronic treatment with AF150(S). Furthermore, prolonged administration of AF150(S) restored cognitive and behavioral impairments in aged microcebes, an animal model that mimics AD pathol. Except M1 agonists, there are no reports on compds. having combined effects, e.g., amelioration of cognition dysfunction and beneficial modulation of APPs together with tau phosphorylation. This unique property of M1 agonists to alter different aspects assocd. with AD pathogenesis could represent the most remarkable, yet unexplored, or even ignored, clin. value of such drugs. Finally, EVOXAC (Cevimeline, AF102B) was recently approved by the FDA for the treatment of dry mouth in Sjogren syndrome, an autoimmune disease that affects exocrine glands.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 26 MEDLINE
ACCESSION NUMBER: 2001137312 MEDLINE
DOCUMENT NUMBER: 21014500 PubMed ID: 11131543
TITLE: Functional **repair** with neural stem cells.
AUTHOR: Sinden J D; Stroemer P; Grigoryan G; Patel S; French S J; Hodges H
CORPORATE SOURCE: ReNeuron Limited, Europoint Centre, 5-11 Lavington Street, London SE1 0NZ, UK.
SOURCE: NOVARTIS FOUNDATION SYMPOSIUM, (2000) 231 270-83; discussion 283-8, 302-6. Ref: 24
Journal code: 9807767.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404

Last Updated on STN: 20010404
Entered Medline: 20010308

AB Approval to commence phase I/II clinical trials with neural stem cells requires proof of concept in well-accepted animal models of human neurological disease or injury. We initially showed that the conditionally immortal MHP36 line of hippocampal origin (derived from the H-2Kb-tsA58 transgenic mouse) was effective in repopulating CA1 neurons in models of global ischaemia and repairing cognitive function, and have now shown that this line is multifunctional. MHP36 cells are effective in restoring spatial **memory deficits** in rats after excitotoxic lesions of the cholinergic projections to cortex and hippocampus and in rats showing cognitive impairments due to normal ageing. Moreover, grafts of MHP36 cells are effective in reversing sensory and motor deficits and reducing lesion volume as a consequence of occlusion of the middle cerebral artery, the major cause of stroke. In contrast, MHP36 cell grafts were unable to **repair** motor asymmetries in rats with unilateral 6-hydroxydopamine lesions of the nigrostriatal dopamine system, the prototype rodent model of Parkinson's disease. These data show that conditionally immortal neuroepithelial stem cells are multifunctional, being able to **repair** diverse types of brain damage. However, there are limitations to this multifunctionality, suggesting that lines from different regions of the developing brain will be required to treat different brain diseases. ReNeuron is currently developing human neuroepithelial stem cell lines from different brain regions and with similar reparative properties to our murine lines.

L11 ANSWER 7 OF 26 MEDLINE
ACCESSION NUMBER: 2000105236 MEDLINE
DOCUMENT NUMBER: 20105236 PubMed ID: 10637467
TITLE: Testosterone supplementation in the aging male.
AUTHOR: Kim Y C
CORPORATE SOURCE: Center for Reproduction and Genetics, and Department of Urology, Pundang Je-Saeng Hospital, Dae-Jin Medical Center, Korea.
SOURCE: INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH, (1999 Dec) 11 (6) 343-52. Ref: 57
Journal code: 9007383. ISSN: 0955-9930.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000217

AB World-wide life expectancy at birth for men and women will have increased by about 20 y during 50 y period between 1950 and 2000. As a result, the proportion of the elderly population is expected to increase significantly in the 21st century. Despite this increase in longevity for men and women, men still have significantly shorter life expectancy of approximately 5 y. To further reduce and prevent debilitating disease and disability in elderly men, a question is whether any type of interventions, such as hormone **replacement** therapy, may play a role in improving the quality of life as proven in post-menopausal women. Men experience age-related decline of capability physically and mentally. Various symptoms, such as nervousness, depression, impaired **memory**, **inability** to concentrate, easy fatigability, insomnia, hot flushes, periodic sweating, reduction of muscle mass and power, bone ache, and sexual dysfunction, are related to this change. The fact that a number of age-related changes resemble features of various hormonal deficiency

has led to worldwide interest in the use of various hormonal preparations in an effort to prevent the aging process in elderly men. Even though there have been opinions against hormonal supplementation in the aging male, preliminary studies defining the risk/benefit ratio of androgen supplementation appear to be encouraging. To understand testosterone supplementation in the aging male, this review will discuss the following important topics: physiology of male hormonal balance, changes in reproductive organs in elderly men, endocrine evaluation of the male, pharmacological effects of testosterone on target organs, available preparations for testosterone, and testosterone supplementation.

L11 ANSWER 8 OF 26 MEDLINE
ACCESSION NUMBER: 1999183642 MEDLINE
DOCUMENT NUMBER: 99183642 PubMed ID: 10083896
TITLE: How much, and by what mechanisms, does growth hormone **replacement** improve the quality of life in GH-deficient adults?.
AUTHOR: Chrisoulidou A; Kousta E; Beshyah S A; Robinson S; Johnston D G
CORPORATE SOURCE: Division of Medicine, Imperial College School of Medicine, St. Mary's Hospital, London, UK.
SOURCE: BAILLIERES CLINICAL ENDOCRINOLOGY AND METABOLISM, (1998 Jul) 12 (2) 261-79. Ref: 52
Journal code: 8704785. ISSN: 0950-351X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990415

AB The majority of studies (but not all) have demonstrated that adults with hypopituitarism of both childhood and adult onset have a diminished quality of life (QOL) in comparison with the normal population. Reductions in physical and mental energy, dissatisfaction with body image and poor memory have been reported most consistently. A specific role for growth hormone (GH) deficiency, as opposed to multiple pituitary hormone deficiency, has been observed for the **memory deficit**, which extends to both short- and long-term memory. Comparisons with normal siblings have confirmed the reduced QOL, although differences have been small. There is less consensus for a reduction in QOL when hypopituitary subjects are compared with patients with other chronic diseases, with studies supporting (in comparison with diabetics) and refuting (in comparison with patients following mastoid surgery) the reduction in QOL. GH **replacement** in adults has improved QOL, particularly in the domains of energy level and self-esteem, and memory has improved. The social impact of these changes may be considerable, with patients requiring fewer days' sick leave. A major placebo effect is present, however, and neutral results as well as positive have been reported in placebo-controlled trials. Where a positive effect has been observed, it has been more likely to occur in patients with a low QOL at the outset. It is otherwise impossible to predict at the outset those who will benefit from GH **replacement**. GH treatment has effects on body composition, exercise capacity, muscle strength, total body water and intermediary metabolism which would be expected to improve QOL. **Replacement** therapy also has side-effects, and it is the variable balance of the positive and negative effects, coupled with the difficulties of measuring QOL, which have led to the disparate results in the literature. There is probably also a true inter-individual variation,

although the mechanisms of this are currently unknown.

L11 ANSWER 9 OF 26 MEDLINE
ACCESSION NUMBER: 1999017950 MEDLINE
DOCUMENT NUMBER: 99017950 PubMed ID: 9799622
TITLE: Estrogen replacement attenuates effects of scopolamine and lorazepam on memory acquisition and retention.
AUTHOR: Gibbs R B; Burke A M; Johnson D A
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Pittsburgh School of Pharmacy, 1004 Salk Hall, Pittsburgh, Pennsylvania, 15261, USA.
CONTRACT NUMBER: 2P30HD08610 (NICHD)
R01-NS28896 (NINDS)
SOURCE: HORMONES AND BEHAVIOR, (1998 Oct) 34 (2) 112-25.
Journal code: 0217764. ISSN: 0018-506X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 19990128
Entered Medline: 19990108

AB A multiple-trial passive avoidance paradigm was used to examine and compare the ability for estrogen **replacement** to attenuate learning and **memory deficits** produced by the muscarinic antagonist scopolamine and the benzodiazepine lorazepam. The multiple-trial paradigm was used in order to distinguish effects on acquisition from effects on retention. Estrogen replacement significantly attenuated a scopolamine-induced deficit on passive avoidance acquisition, but not retention. The ability for estrogen to attenuate the effect of scopolamine on acquisition was observed only when the analysis was limited to animals with serum levels of estradiol <200 pg/ml, suggesting that higher levels of estradiol were ineffective. This observation is consistent with at least one recent study showing dose-related effects of estrogen on ChAT-like immunoreactivity in the basal forebrain and supports the hypothesis that effects of estrogen on basal forebrain cholinergic neurons can help to reduce cognitive deficits associated with cholinergic impairment. Estrogen replacement was also observed to protect against a lorazepam-induced impairment on passive avoidance retention. This effect was observed specifically in animals that received estrogen prior to and during training and was not due to any effect of estrogen on serum levels of lorazepam following acute lorazepam administration. Collectively, these data demonstrate the ability for estrogen replacement to attenuate specific pharmacologically induced impairments in learning and retention and provide additional clues as to potential mechanisms by which estrogen replacement may help to reduce cognitive deficits associated with aging and Alzheimer's disease in postmenopausal women.

L11 ANSWER 10 OF 26 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:75571 CA
TITLE: Mechanisms of noradrenergic modulation of physical therapy: effects on functional recovery after cortical injury
AUTHOR(S): Feeney, Dennis M.
CORPORATE SOURCE: Departments of Psychology and Neurosciences, University of New Mexico, Albuquerque, NM, USA
SOURCE: Restorative Neurology (1998), 35-78. Editor(s): Goldstein, Larry B. Futura: Armonk, N. Y.
CODEN: 66UYAI
DOCUMENT TYPE: Conference; **General Review**

LANGUAGE: English

AB A review with 190 refs. The possibility for increasing the ultimate level of functional recovery late after cortical injury by NA/PT has been demonstrated in several models and species and by preliminary data in stroke patients. These initial studies combined pharmacol. increases in central NA with PT given during the period of drug action. Alleviation of deficits included transient restoration of absent reflexes, enhanced recovery of locomotion, recovery of stereopsis, and recovery of spatial learning and **memory deficits** after cortical ablation in models of stroke or cerebral trauma. Conversely, blocking .alpha.1-NA receptors retards recovery and reinstates symptoms in apparently recovered animals, further supporting an important role for NA in functional recovery. The long therapeutic window of weeks to months of this NA/PT strategy indicates it affects neurons rendered dysfunctional by cerebral injury. The current hypotheses of the mechanisms of this exptl. treatment are that increasing neuronal and glial metab. **restores** homeostasis in dysfunctional cells or reestablishes disturbed excitatory/inhibitory imbalance. Furthermore, this mechanism provides a new focus for therapy, by normalizing otherwise dysfunctional neurons. This body of work represents a beginning of exptl. rehabilitation pharmacol. for treating patients previously thought untreatable.

REFERENCE COUNT: 190 THERE ARE 190 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 26 MEDLINE

ACCESSION NUMBER: 97276551 MEDLINE

DOCUMENT NUMBER: 97276551 PubMed ID: 9130304

TITLE: Cognitive deficits induced by global cerebral ischaemia: prospects for transplant therapy.

AUTHOR: Hodges H; Nelson A; Virley D; Kershaw T R; Sinden J D

CORPORATE SOURCE: Department of Psychology, Institute of Psychiatry, London, UK.

SOURCE: PHARMACOLOGY, BIOCHEMISTRY AND BEHAVIOR, (1997 Apr) 56 (4) 763-80. Ref: 153
Journal code: 0367050. ISSN: 0091-3057.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199707

ENTRY DATE: Entered STN: 19970721
Last Updated on STN: 20000303
Entered Medline: 19970707

AB Global ischaemia induced by interruption of cerebral blood flow results in damage to vulnerable cells, notably in the CA1 and hilar hippocampal fields, and is frequently associated with **memory deficits**. This review examines cognitive deficits that occur in animal models of global ischaemia in rats and monkeys, the extent to which these deficits are associated with CA1 cell loss, and the evidence for functional recovery following transplants of foetal CA1 cells and grafts of conditionally immortalised precursor cells. In rats, impairments are seen most consistently in tasks of spatial learning and spatial working memory dependent on use of allocentric environmental cues. In monkeys, ischaemic deficits have been shown to a moderate extent in delayed object recognition tasks, but animals with a selective excitotoxic CA1 lesion show a profound impairment in conditional discrimination tasks, suggesting that these may be a more sensitive measure of ischaemic impairments. Several studies have reported correlational links between the extent of CA1 cell loss following two or four vessel occlusion (2 VO, 4 VO) in rats

and behavioural impairments, but recent findings indicate that at intermediate levels of damage these relationships are weak and variable, and emerge clearly only when animals with maximal CA1 cell loss are included, suggesting that the deficits involve more than damage to the CA1 field. Nevertheless, ischaemic rats and CA1-lesioned marmosets with grafts of foetal CA1 cells show substantial improvements; in rats these are not found with grafts from other hippocampal fields. Conditionally immortalised cell lines and trophic grafts are currently being assessed for their functional potential in animal models, because clinical use of foetal cells will not be practicable. Recent findings suggest that an expanded population of neuroepithelial cells derived from the conditionally immortalised H-2Kb-tsA58 transgenic mouse improve spatial learning as effectively as CA1 foetal grafts in rats subjected to 4 VO, and clonal lines from the same source show similar promise. Lines derived from precursor cells have the potential to develop into different types of cell (neuronal or glial) depending on signals from the host brain. These cell lines may therefore have the capacity to **repair** damaged host circuits more precisely than is possible with foetal grafts, and offer a promising, approach both to functional recovery and to elucidating graft-host interactions.

L11 ANSWER 12 OF 26 MEDLINE
ACCESSION NUMBER: 1998031201 MEDLINE
DOCUMENT NUMBER: 98031201 PubMed ID: 9364618
TITLE: Verbal memory after three months of intranasal vasopressin in healthy old humans.
AUTHOR: Perras B; Droste C; Born J; Fehm H L; Pietrowsky R
CORPORATE SOURCE: Department of Clinical Neuroendocrinology, University of Lubeck, Germany.
SOURCE: PSYCHONEUROENDOCRINOLOGY, (1997 Aug) 22 (6) 387-96. Journal code: 7612148. ISSN: 0306-4530.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980122 Last Updated on STN: 19980122 Entered Medline: 19980107

AB In animals, evidence has been accumulated that vasopressin (VP) improves learning and memory. In humans, this effect was not consistently demonstrated, and attempts to **restore** age-related **memory deficits** by VP also remained inconsistent. Assuming that in old subjects a beneficial effect on memory occurs only after prolonged treatment with VP, we conducted a study in 26 healthy elderly persons receiving 40 IU of VP for three months through the intranasal route. The trial was randomized, placebo-controlled and held double-blind. Memory was assessed by the Auditory Verbal Learning Test (AVLT) requiring the subject to learn repeatedly presented lists of 15 words. Results demonstrated no general effect of long-term treatment with VP on memory in aged humans. However, recall of an interfering word list was improved, indicating a diminished proactive interference by the peptide. Additionally, VP influenced recall depending on the serial position of an item: it improved the primacy effect (i.e. recall of the first words of a list) and impaired the recency effect. This result may indicate an improved semantic encoding (i.e. a primary effect on processes of attention) after long-term administration of VP.

L11 ANSWER 13 OF 26 MEDLINE
ACCESSION NUMBER: 1998003088 MEDLINE

DOCUMENT NUMBER: 98003088 PubMed ID: 9344403
TITLE: Role of estrogen **replacement** therapy in memory enhancement and the prevention of neuronal loss associated with Alzheimer's disease.
AUTHOR: Simpkins J W; Green P S; Gridley K E; Singh M; de Fiebre N C; Rajakumar G
CORPORATE SOURCE: Department of Pharmacodynamics and Center for the Neurobiology of Aging, University of Florida, Gainesville 32610, USA.
CONTRACT NUMBER: AG 10485 (NIA)
SOURCE: AMERICAN JOURNAL OF MEDICINE, (1997 Sep 22) 103 (3A) 19S-25S. Ref: 35
Journal code: 0267200. ISSN: 0002-9343.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971104

AB Recent evidence supports a role for estrogens in both normal neural development and neuronal maintenance throughout life. Women spend 25-33% of their life in an estrogen-deprived state and retrospective studies have shown an inverse correlation between dose and duration of estrogen **replacement** therapy (ERT) and incidence of Alzheimer's disease (AD), suggesting a role for estrogen in the prevention and/or treatment of neurodegenerative diseases. To explore these observations further, an animal model was developed using ovariectomy (OVX) and ovariectomy with estradiol **replacement** (E2) in female Sprague-Dawley rats to mimic postmenopausal changes. Using an active-avoidance paradigm and a spatial memory task, the effects of estrogen deprivation were tested on memory-related behaviors. OVX caused a decline in avoidance behavior, and estrogen **replacement** normalized the response. In the Morris water task of spatial memory, OVX animals showed normal spatial learning but were **deficient** in spatial **memory**, an effect that was prevented by estrogen treatment. Together these data indicate that OVX in rats results in an estrogen-reversible impairment of learning/memory behavior. Because a plethora of information has been generated that links decline in memory-related behavior to dysfunction of cholinergic neurons, the effects of estrogens on cholinergic neurons were tested. We demonstrated that OVX causes a decrease in high affinity choline uptake and choline acetyltransferase activity in the hippocampus and frontal cortex; ERT reverses this effect. Further, we showed that estrogens promote the expression of mRNA for brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF), 2 neurotrophic substances that have been shown to ameliorate the effects of age and injury on cholinergic neurons. Tissue culture models were used to evaluate whether estrogen treatment increases the survival of neurons when exposed to a variety of insults. 17-beta-Estradiol (beta-E2) protects cells from the neurotoxic effects of serum deprivation and hypoglycemia in human neuroblastoma cell lines. We have also observed that 17-alpha-estradiol (alpha-E2), a weak estrogen, shows neuroprotective efficacy in the SK-N-SH cell line at concentrations equivalent to beta-E2. Finally, we have observed that tamoxifen, a classic estrogen antagonist, blocks only one-third of the neuroprotective effects of either alpha-E2 or beta-E2. Collectively, these results indicate that estrogen is behaviorally active in tests of learning/ memory; activates basal forebrain cholinergic neurons and neurotrophin expression; and is neuroprotective for human neuronal cultures. We conclude that estrogen may be a useful therapy for AD and

other neurodegenerative diseases.

L11 ANSWER 14 OF 26 MEDLINE
ACCESSION NUMBER: 1998003087 MEDLINE
DOCUMENT NUMBER: 98003087 PubMed ID: 9344402
TITLE: Estrogen, cognition, and a woman's risk of Alzheimer's disease.
AUTHOR: Henderson V W
CORPORATE SOURCE: Department of Neurology, University of Southern California, and the Los Angeles County-University of Southern California Medical Center, 90033, USA.
SOURCE: AMERICAN JOURNAL OF MEDICINE, (1997 Sep 22) 103 (3A) 11S-18S. Ref: 100
Journal code: 0267200. ISSN: 0002-9343.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971104

AB Alzheimer's disease affects women more often than men, and women with this form of dementia show greater naming (semantic **memory**) **deficits** during the course of their illness. Gonadal steroids exert organizational and activational effects on central nervous system neurons and influence brain function in other important ways. Several estrogenic actions are potentially relevant to Alzheimer's disease, and it is hypothesized that one consequence of estrogen deprivation after the menopause is a higher risk of this dementing disorder. In healthy women without dementia, estrogen may enhance cognitive performance, especially in the domain of verbal memory, although the magnitude of such effects is small. Several small treatment trials of estrogen **replacement** in women with Alzheimer's disease, however, suggest that estrogen's effects on cognition could be larger in this population and may be most apparent on tasks of semantic memory. Analyses in voluntary cohorts associate postmenopausal estrogen **replacement** therapy with a lower risk of subsequent Alzheimer's disease. In 3 recent epidemiologic studies, information on postmenopausal estrogen use was collected prospectively; while inconclusive, findings raise the possibility that postmenopausal estrogen **replacement** reduces a woman's risk of subsequent dementia. New information from basic research and from large randomized treatment studies, cohort studies, and case-control studies is needed to resolve important unanswered clinical issues.

L11 ANSWER 15 OF 26 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:357429 CA
TITLE: Estrogen, cognition, and a woman's risk of Alzheimer's disease
AUTHOR(S): Henderson, Victor W.
CORPORATE SOURCE: Departments of Neurology (Division of Cognitive Neuroscience and Neurogerontology) and Psychology, School of Gerontology, and Program in Neural, Informational, and Behavioral Sciences, University of Southern California, Los Angeles, CA, 90033, USA
SOURCE: American Journal of Medicine (1997), 103(3(A)), 11S-18S
CODEN: AJMEAZ; ISSN: 0002-9343
PUBLISHER: Excerpta Medica
DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review, with 100 refs. Alzheimer's disease affects women more often than men, and women with this form of dementia show greater naming (semantic **memory**) **deficits** during the course of their illness. Gonadal steroids exert organizational and activational effects on central nervous system neurons and influence brain function in other important ways. Several estrogenic actions are potentially relevant to Alzheimer's disease, and it is hypothesized that one consequence of estrogen deprivation after the menopause is a higher risk of this dementing disorder. In healthy women without dementia, estrogen may enhance cognitive performance, esp. in the domain of verbal memory, although the magnitude of such effects is small. Several small treatment trials of estrogen **replacement** in women with Alzheimer's disease, however, suggest that estrogen's effects on cognition could be larger in this population and may be most apparent on tasks of semantic memory. Analyses in voluntary cohorts assoc. postmenopausal estrogen **replacement** therapy with a lower risk of subsequent Alzheimer's disease. In 3 recent epidemiol. studies, information on postmenopausal estrogen use was collected prospectively; while inconclusive, findings raise the possibility that postmenopausal estrogen **replacement** reduces a woman's risk of subsequent dementia. New information from basic research and from large randomized treatment studies, cohort studies, and case-control studies is needed to resolve important unanswered clin. issues.

L11 ANSWER 16 OF 26 MEDLINE

ACCESSION NUMBER: 97004602 MEDLINE
DOCUMENT NUMBER: 97004602 PubMed ID: 8851913
TITLE: Neural grafting of cholinergic neurons in the hippocampal formation.
AUTHOR: Tarricone B J; Simon J R; Li Y J; Low W C
CORPORATE SOURCE: Institute of Psychiatric Research, Medical Neurobiology, Indiana University School of Medicine, Indianapolis 46202, USA.
CONTRACT NUMBER: RO1-NS-24464 (NINDS)
SOURCE: BEHAVIOURAL BRAIN RESEARCH, (1996 Jan) 74 (1-2) 25-44. Ref: 121
Journal code: 8004872. ISSN: 0166-4328.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961205

AB The cholinergic septohippocampal system plays an important role in spatial learning and memory functions. Transections of the septohippocampal pathway have been shown to result in a near complete loss of cholinergic innervation in the hippocampus and induce severe spatial memory impairments. In this article, we have reviewed the studies which demonstrate the ability of intrahippocampal septal grafts to reinnervate the hippocampal formation and ameliorate spatial learning and **memory deficits**. Neuroanatomical studies suggest that grafts of cholinergic tissue can innervate the host hippocampal formation in a pattern that mimics that of the normal septohippocampal pathway. This innervation, in turn, is associated with the formation of graft-to-host synaptic connections. Neurochemical studies reveal that intrahippocampal grafts of septal cells can **restore** choline acetyltransferase activity, acetylcholine synthesis, and high affinity choline uptake in

presynaptic terminals of grafted neurons. In addition, these grafts can normalize the upregulation of cholinergic muscarinic receptors seen postsynaptically in the hippocampus following lesions of the septohippocampal pathway. The functional nature of these grafts is also substantiated by electrophysiological recordings which demonstrate stimulus-evoked graft-to-host synaptic transmission as well as the reinstatement of EEG activity typical of septohippocampal connectivity. In addition to graft-to-host connections, behavioral and neurochemical studies also provide evidence for host-to-graft connections that can regulate the activity of grafted cholinergic neurons during the performance of specific behavioral tasks requiring spatial memory function. Together, these studies suggest that grafts of cholinergic neurons from the medial septal nucleus can become anatomically and functionally incorporated into the circuitry of the host hippocampal formation.

L11 ANSWER 17 OF 26 MEDLINE
ACCESSION NUMBER: 95391919 MEDLINE
DOCUMENT NUMBER: 95391919 PubMed ID: 7662912
TITLE: Tolcapone, an inhibitor of catechol O-methyltransferase, counteracts memory deficits caused by bilateral cholinotoxin lesions of the basal nuclei of Meynert.
AUTHOR: Khromova I; Rauhala P; Zolotov N; Mannisto P T
CORPORATE SOURCE: University of Helsinki, Department of Pharmacology and Toxicology, Finland.
SOURCE: NEUROREPORT, (1995 May 30) 6 (8) 1219-22.
Journal code: 9100935. ISSN: 0959-4965.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951020
Last Updated on STN: 19980206
Entered Medline: 19951010

AB Repeated administration of tolcapone, an inhibitor of catechol-O-methyltransferase, was able to partially **restore** the **memory deficits** caused by bilateral cholinotoxin (AF64A) lesions in the basal magnocellular nuclei of Meynert. The 2-week tolcapone treatment (3 mg kg-1, once a day) was started 24 h before toxin infusion and the last injection was given 24 h before the first avoidance test. The beneficial action of tolcapone may be related to antioxidant properties of nitrocatechols.

L11 ANSWER 18 OF 26 MEDLINE
ACCESSION NUMBER: 95295829 MEDLINE
DOCUMENT NUMBER: 95295829 PubMed ID: 7777056
TITLE: Essential role of neocortical acetylcholine in spatial memory.
COMMENT: Comment in: Nature. 1995 Jun 8;375(6531):446
AUTHOR: Winkler J; Suhr S T; Gage F H; Thal L J; Fisher L J
CORPORATE SOURCE: Department of Neurosciences, University of California, San Diego, La Jolla 92093, USA.
SOURCE: NATURE, (1995 Jun 8) 375 (6531) 484-7.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199507
ENTRY DATE: Entered STN: 19950720
Last Updated on STN: 19950720

Entered Medline: 19950710

AB The cholinergic system plays a crucial role in learning and memory. Lesions of cholinergic nuclei, pharmacological manipulations of cholinergic systems, intracerebral transplantation of fetal tissue and anatomical changes in cholinergic pathways during ageing have all been correlated with altered cognitive behaviour. However, it has not been proved that regional acetylcholine is causally required for learning and memory. Here we describe how we achieved a permanent and selective impairment of learning and memory by damaging the nucleus basalis magnocellularis, a nucleus that provides the major cholinergic innervation of the neocortex, in adult rats. To test the hypothesis that acetylcholine is essential for restoration of cognitive function, we implanted genetically modified cells that produce acetylcholine into denervated neocortical target regions. After grafting, rats with increased neocortical acetylcholine levels showed a significant improvement in a spatial navigation task. Acetylcholine is thus not only necessary for learning and memory, as previously argued, but its presence within the neocortex is also sufficient to ameliorate learning **deficits** and **restore memory** following damage to the nucleus basalis.

L11 ANSWER 19 OF 26 MEDLINE
ACCESSION NUMBER: 96156470 MEDLINE
DOCUMENT NUMBER: 96156470 PubMed ID: 8584241
TITLE: AIT-082, a unique purine derivative, enhances nerve growth factor mediated neurite outgrowth from PC12 cells.
AUTHOR: Middlemiss P J; Glasky A J; Rathbone M P; Werstuik E; Hindley S; Gysbers J
CORPORATE SOURCE: Department of Biomedical Sciences, McMaster University, Hamilton, Ontario, Canada.. middlems@fhs.csu.mcmaster.ca
CONTRACT NUMBER: AG09911 (NIA)
SOURCE: NEUROSCIENCE LETTERS, (1995 Oct 20) 199 (2) 131-4. Journal code: 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960327
Last Updated on STN: 19970203
Entered Medline: 19960320

AB AIT-082 is a novel, metabolically stable, derivative of the purine hypoxanthine. Addition of AIT-082 to cultured PC12 cells enhanced significantly nerve growth factor (NGF)-mediated neurite outgrowth from PC12 cells. These results suggest a cellular mechanism, the enhancement of NGF-action, that might account for the ability of AIT-082 to **restore** age-induced working **memory deficits** in mice.

L11 ANSWER 20 OF 26 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:510290 BIOSIS
DOCUMENT NUMBER: PREV199497523290
TITLE: AIT-082 modulates neuritogenesis through a carbon monoxide/guanylate cyclase mechanism and **restores** age-induced **memory deficits**.
AUTHOR(S): Glasky, A. J. (1); Ritzmann, R. F.; Melchior, C. L.; Hindley, S.; Gysbers, J. W.; Middlemiss, P.; Rathbone, M. P.
CORPORATE SOURCE: (1) Adv. ImmunoThera-peutics, Tustin, CA 92680 USA
SOURCE: Society for Neuroscience Abstracts, (1994) Vol. 20, No. 1-2, pp. 1099.
Meeting Info.: 24th Annual Meeting of the Society for Neuroscience Miami Beach, Florida, USA November 13-18, 1994

ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English

L11 ANSWER 21 OF 26 MEDLINE
ACCESSION NUMBER: 93226658 MEDLINE
DOCUMENT NUMBER: 93226658 PubMed ID: 8469692
TITLE: Effect of age and strain on working memory in mice as measured by win-shift paradigm.
AUTHOR: Ritzmann R F; Kling A; Melchior C L; Glasky A J
CORPORATE SOURCE: Advanced Immuno Therapeutics, Irvine, CA 92680.
CONTRACT NUMBER: NIA 09911 (NIAAA)
NIAAA 08709
SOURCE: PHARMACOLOGY, BIOCHEMISTRY AND BEHAVIOR, (1993 Apr) 44 (4) 805-7.
Journal code: 0367050. ISSN: 0091-3057.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930521
Last Updated on STN: 19960129
Entered Medline: 19930511

AB Working memory is disrupted in Alzheimer's disease and stroke; therefore, any therapeutic drug should **restore deficits** in working **memory**. The win-shift foraging paradigm has been demonstrated to be a model of working memory in rats. In the present study, this paradigm was adapted to mice because of the greater ease and economy of testing potential drugs in mice and the wider availability of strains of aged mice with naturally occurring working memory deficits. This study has demonstrated strain differences in the working memory trace and that age induces a deficit that can be detected at 11 months of age in mice. Tacrine and physostigmine enhance the memory trace in normal mice and physostigmine can reverse age-induced working memory deficits in subjects with mild and moderate deficits but not in subjects with severe deficits.

L11 ANSWER 22 OF 26 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 118:160901 CA
TITLE: Pharmacological effects of phosphatidylserine in the aging rat brain
AUTHOR(S): Nunzi, Maria Grazia; Toffano, Gino
CORPORATE SOURCE: Fidia Res. Lab., Abano Terme, 35031, Italy
SOURCE: Advances in Behavioral Biology (1992), 40(Treat. Dementias), 199-205
CODEN: ADBBBW; ISSN: 0099-6246
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Treatments with BC-PS increases learning and memory function in aged rodents and prevents the age-assocd. decay in avoidance. The authors report that chronic oral BC-PS administration **restores**, in aged rodents, both spatial **memory deficits** and the underlying neuroanatomical pathways affected by the aging process. In summary, long-term oral BC-PS administration restores biochem. properties of cholinergic neurons in the septo-hippocampal system, enhances hippocampal synaptic plasticity and improves cognitive functions in aged memory-impaired rats. Since BC-PS treatment prevents or restores biol. and behavioral deficits assocd. with the aging process in exptl. animals, this phospholipid represents a possible therapeutic agent for memory dysfunctions in the elderly.

L11 ANSWER 23 OF 26 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1990:54075 BIOSIS
DOCUMENT NUMBER: BA89:31439
TITLE: AMNESIA AND MEMORY FOR MODALITY INFORMATION.
AUTHOR(S): PICKERING A D; MAYES A R; FAIRBAIRN A F
CORPORATE SOURCE: DEP. PSYCHOL. ST. GEORGE'S HOSP. MED. SCH., CRANMER TERRACE, LONDON SW17, UK.
SOURCE: NEUROPSYCHOLOGIA, (1989) 27 (10), 1249-1260. CODEN: NUPSA6. ISSN: 0028-3932.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB In this study, lists of words were used in a mixed-modality fashion (some read aloud by the subject, others read only by the experimenter). They were presented in this format to both Korsakoff amnesics and matched controls, with subjects only told to remember the words themselves. Controls and amnesics were matched on item-memory (forced-choice recognition) by using longer lists, tested at longer delays, for the controls. Despite this, however, the controls performed significantly better than the amnesics at modality-identification judgements about the items chosen during recognition. Whether the **replaced** result reflects the **memory deficit** which causes amnesia, or whether it is more properly attributed to additional (frontal lobe) pathology present in only certain amnesics, is discussed.

L11 ANSWER 24 OF 26 MEDLINE
ACCESSION NUMBER: 90001396 MEDLINE
DOCUMENT NUMBER: 90001396 PubMed ID: 2675993
TITLE: Restoration of memory following septo-hippocampal grafts: a possible treatment for Alzheimer's disease.
AUTHOR: Bond N W; Walton J; Pruss J
CORPORATE SOURCE: School of Behavioural Sciences, Macquarie University, Sydney, New South Wales, Australia.
SOURCE: BIOLOGICAL PSYCHOLOGY, (1989 Feb) 28 (1) 67-87. Ref: 60 Journal code: 0375566. ISSN: 0301-0511.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) **General Review; (REVIEW)** (REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198911
ENTRY DATE: Entered STN: 19900328 Last Updated on STN: 19980206 Entered Medline: 19891109

AB The present paper outlines the reasons for the current interest in work on septo-hippocampal grafts. It examines the role of cholinergic dysfunction in the **memory deficits** associated with Alzheimer's disease, the effects of hippocampal lesions on memory in infra-human animals, and the anatomy of the hippocampus. Methodological aspects of neural grafting are then examined, including the source, nature and site of the graft. A review of the tasks employed to determine functional recovery following septo-hippocampal grafts suggests that although recovery is evident its nature is unclear. An experiment is described which suggests that grafts from embryonic septum bring about recovery of working memory in rats. Different bases of the recovery of function are discussed, including the role of the graft in eliciting release of trophic factors from the host brain; the possibility that the graft acts by providing a pool of neurotransmitter; and finally that the graft may **replace** the damaged circuitry of the host. Some problems of the grafting procedure are outlined. It is concluded that grafting may provide a viable treatment technique in the absence of other forms of treatment for Alzheimer's disease.

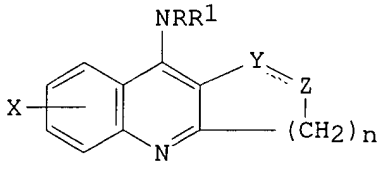
L11 ANSWER 25 OF 26 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 105:172311 CA
TITLE: 9-Amino-1,2,3,4-tetrahydroacridin-1-ol and related compounds, and their use as medicaments
INVENTOR(S): Shutske, Gregory M.; Pierrat, Frank A.
PATENT ASSIGNEE(S): Hoechst-Roussel Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 102 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 179383	A2	19860430	EP 1985-113041	19851015
EP 179383	A3	19870128		
EP 179383	B1	19910529		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4631286	A	19861223	US 1984-664731	19841025
US 4695573	A	19870922	US 1985-781155	19851001
HU 41009	A2	19870330	HU 1985-4042	19851012
HU 196183	B	19881028		
AT 63903	E	19910615	AT 1985-113041	19851015
FI 8504156	A	19860426	FI 1985-4156	19851023
FI 86421	B	19920515		
FI 86421	C	19920825		
ES 548137	A1	19861116	ES 1985-548137	19851023
IL 76796	A1	19900319	IL 1985-76796	19851023
IL 90300	A1	19901129	IL 1985-90300	19851023
DK 8504888	A	19860426	DK 1985-4888	19851024
DK 167250	B1	19930927		
NO 8504261	A	19860428	NO 1985-4261	19851024
NO 169121	B	19920203		
NO 169121	C	19920513		
AU 8549038	A1	19860501	AU 1985-49038	19851024
AU 589141	B2	19891005		
ZA 8508163	A	19860625	ZA 1985-8163	19851024
JP 61148154	A2	19860705	JP 1985-236541	19851024
JP 05041141	B4	19930622		
CA 1292744	A1	19911203	CA 1985-493743	19851024
ES 554569	A1	19880101	ES 1986-554569	19860430
ES 554568	A1	19880516	ES 1986-554568	19860430
US 4839364	A	19890613	US 1987-7885	19870128
US 4754050	A	19880628	US 1987-125526	19871125
US 4835275	A	19890530	US 1987-125109	19871125
JP 01125362	A2	19890517	JP 1988-203316	19880817
JP 05084306	B4	19931201		
AU 8938234	A1	19891026	AU 1989-38234	19890719
AU 615768	B2	19911010		
NO 9004711	A	19860428	NO 1990-4711	19901030
NO 172847	B	19930607		
NO 172847	C	19930915		
DK 9201419	A	19921126	DK 1992-1419	19921126
DK 168704	B1	19940524		

PRIORITY APPLN. INFO.:

US 1984-664731	19841025
US 1985-781155	19851001
EP 1985-113041	19851015
IL 1985-76796	19851023
NO 1985-4261	19851024
US 1987-7885	19870128

OTHER SOURCE(S): CASREACT 105:172311
GI



I

AB The title compds. I (R = H, alkyl; R1 = H, alkyl, arylalkyl, diarylalkyl, heterocyclylalkyl, etc.; X = H, alkyl, alkoxy, halo, OH, etc.; Y = CO, CR3OH, R3 = H, alkyl; X = CH2, C:CR4R5, R4, R5 = H, alkyl; YZ = CR3:CH, CR3 and CH = Y and Z, resp.; n = 1-3) and their salts, useful in treatment of various memory dysfunctions characterized by decreased cholinergic function, were prepd. Thus, anthranilonitrile was reacted with 1,3-cyclohexanedione to give 2-(3-oxocyclohexen-1-yl)aminobenzonitrile as the HCl salt which was cyclized in presence of K2CO3 and CuCl to 9-amino-3,4-dihydroacridin-1(2H)-one which was reduced with LiAlH4 in Et2O to 9-amino-1,2,3,4-tetrahydroacridin-1-ol (II). In cholinesterase inhibition assay by a photometric method II had an IC50 of 2.3 .times. 10-5M and in the Dark Avoidance Assay to **restore** cholinergically **deficient memory** in mice, II was effective at 0.63 mg/kg.

L11 ANSWER 26 OF 26 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1984:97228 BIOSIS
DOCUMENT NUMBER: BR27:13720
TITLE: REVERSIBLE STEROID DEMENTIA IN PATIENTS WITHOUT STEROID PSYCHOSIS.
AUTHOR(S): VARNEY N R; ALEXANDER B; MACINDOE J H
CORPORATE SOURCE: PSYCHOL. SERVICE, VA MED. CENT., IOWA CITY, IOWA 52240.
SOURCE: Am. J. Psychiatry, (1984) 141 (3), 369-372.
CODEN: AJPSAO. ISSN: 0002-953X.
FILE SEGMENT: BR; OLD
LANGUAGE: English